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MEDICAL AND SURGICAL REPORTS

OF

THE BOSTON CITY HOSPITAL.

Ninth Series.

EDITED BY

CHARLES F. FOLSOM, M.D., W. T. COUNCILMAN, M.D.,
AND HERBERT L. BURRELL, M.D.

BOSTON:
PUBLISHED BY THE TRUSTEES.
1898.

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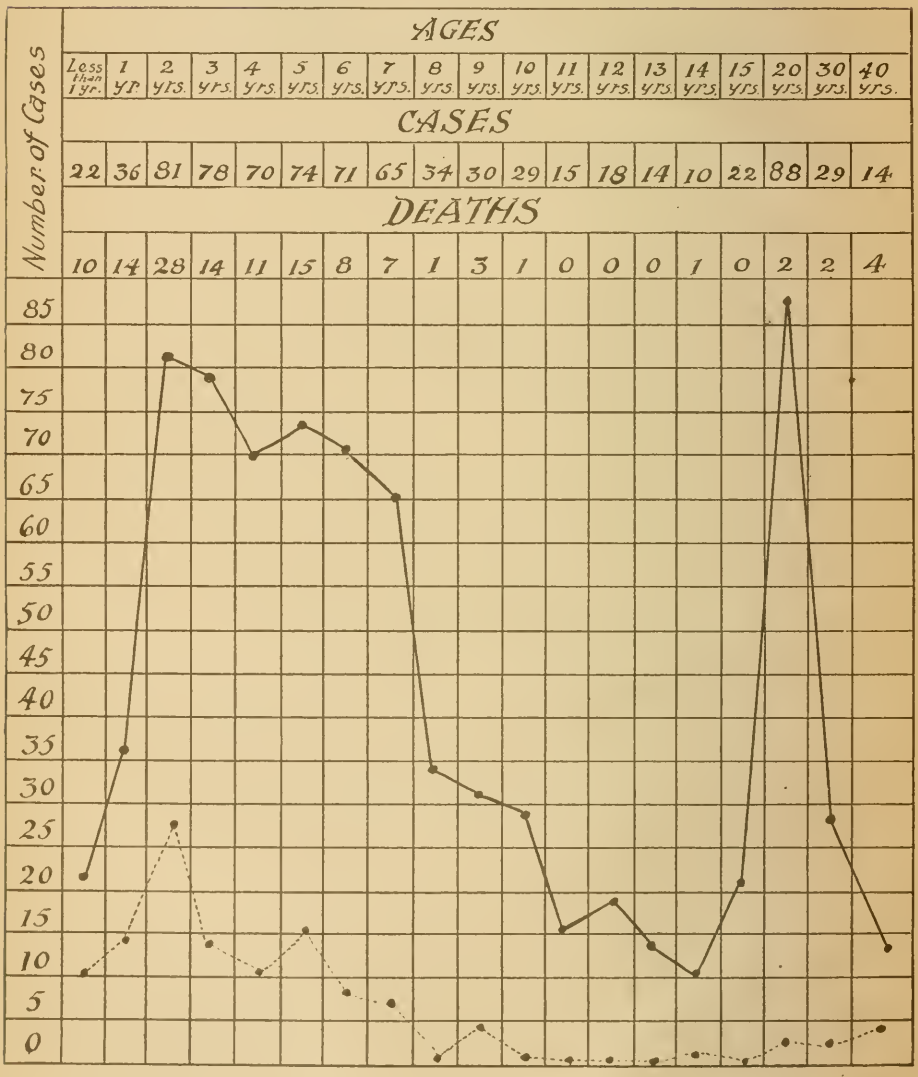
CHART SHOWING THE CASES OF DIPHTHERIA, AND THE DEATHS, WITH THE AGE.

Cases: ——————

Deaths: ....



I.

A CLINICAL STUDY OF EIGHT HUNDRED CASES OF DIPHTHERIA AT THE SOUTH DEPARTMENT OF THE BOSTON CITY HOSPITAL.

By John H. McCollom, M.D., *Resident Physician.*

These 800 cases were all of them diphtheria, both from a clinical and from a bacteriological point of view. The different phases that diphtheria may assume, after the subsidence of the acute symptoms, are of interest to the clinician, not only from their bearing on treatment but also from their relation to prognosis. It is now generally conceded that diphtheria is, at the outset, a local disease, and that the constitutional manifestations are due either to the absorbtion of the toxin generated by the growth of the bacilli, or to a mixed infection in which streptococci play an important part.

A study of the accompanying chart shows that the disease is much more prevalent before puberty than after. It will be seen that of the 800 cases 669, or about eighty-three per cent. of the whole number, occurred in children fifteen years of age and under; while in persons over fifteen there were only 131 cases, or about sixteen per cent. The highest death-rate was in infants under one year, being forty-five per cent.; the next highest in children between one and two years, being thirty-nine per cent. The number of cases occurring in children between two and three years of age was the largest in any one year of life, under fifteen years being eighty-one, and the death-rate was thirty-five per cent. Over four years of age the death-rate shows a remarkable diminution each year of life up to fifteen. After fifteen years the death-rate has been estimated at intervals of ten years, and it has been found that during these epochs of life there were 131 cases, as has been before stated, with a death-rate of sixteen per cent. The death-rate in persons forty years old is

quite high, being twenty-nine per cent. higher than that of any age of three years and over. It is a notable fact that in children from ten to fifteen years of age there were seventy-nine cases and only two deaths.

The accompanying table shows the relative frequency of diphtheria in males and females. It will be seen from this table that, while the susceptibility to the disease is greater in females than in males, the death-rate in the former is considerably lower than in the latter. There seems to be no satisfactory explanation of this fact. In the earlier years of life sex certainly can have no influence on the susceptibility to disease, neither can it have any effect on the resisting power of the individual. In the first five years of life the difference between the death-rate of the sexes is very marked, being 30.2 per cent. in males, and 20.4 per cent. in females. From five to ten years the death-rate in males is 10.8 per cent., and that of females is 7; from ten to fifteen years the rate for males is 3.33, while that of females of a corresponding age, comprising forty-nine cases, the death-rate is 0. Over fifteen years of age the death-rate for males is 8 per cent., while that of females is 4 per cent. A marked difference. Lennox Browne in his work, entitled "Diphtheria and its Associates," gives an analysis of 1,000 cases, in which he states that the percentage of mortality in males under five years of age is 45.2, in females 44.5. Between five and ten years, males 22.3 per cent., females 30.3; between ten and fifteen years, males 16.3, females 7.5; and over fifteen years, males 4.4, females 3.6 per cent. The percentage of mortality at the South Department of the whole number of males is 19.67, and that of females, 11.24, as compared with that of 30.3 per cent. in males and 25.9 per cent. in females in Browne's table.

Table of Eight Hundred Cases of Diphtheria, by Sex and by Age, with the Deaths.

Years.	Males.	Deaths.	Females.	Deaths.
Less than 1 year.....	13	7	9	3
1 "	21	9	15	5
2 years.....	44	18	37	10
3 "	40	11	38	3
4 "	30	5	40	6
5 "	37	6	37	9
6 "	35	6	36	2
7 "	34	2	31	5
8 "	11	1	23	–
9 "	11	2	19	1
10 "	10	–	19	1
11 "	3	–	12	–
12 "	8	–	10	–
13 "	6	–	8	–
14 "	4	1	6	–
15 "	9	–	13	–
20 "	38	2	50	–
30 "	15	2	14	–
40+ "	4	1	10	3
	373	73	427	48

Males.....373 with 73 deaths.
Females .....427 " 48 "
800 121

Total, 800 cases, with 121 deaths.
Percentage of mortality, 15.1.

A tabular statement of the 121 fatal cases is appended, showing the age, sex, maximum pulse-rate, maximum temperature, condition of the heart, situation of the membrane, presence of a nasal discharge, existence of laryngeal stenosis, occurrence of septic odor, condition of the cervical glands, ear symptoms, duration of illness at time of entrance, number of days in hospital, and cause of death. There were seventy-one autopsies.

It will be seen from this table that the pulse-rate in the fatal cases was extremely high, the highest being 180, the lowest 100, with an average of 142. A low pulse-rate is frequently found in the course of the disease in a fatal case, but this symptom was observed in only a few instances in this series of cases. The temperature, as a rule, was not specially elevated. The highest temperature noted was 107° F.; the lowest 97°, with an average of 100°. The relation of the pulse to the temperature has a very important bearing on prognosis; a high pulse-rate and a low temperature being symptoms of the gravest import. A marked elevation of temperature in diphtheria indicates some complication, generally broncho-pneumonia. In the only instance where the temperature was 107° the autopsy revealed membrane in the nasal passages, larynx, trachea and bronchi. Broncho-pneumonia was also found, and a streptococcus infection. In the case where the temperature was 106° F., there was no autopsy, but the physical signs were those of broncho-pneumonia. In the first case where the temperature was 105° F., at the autopsy the œsophagus was found to be deeply injected throughout its whole length, denuded of its mucous membrane and covered in irregular longitudinal patches with a thin, dirty yellow membrane, which peeled off easily. Bacilli of diphtheria were not found in the stained sections. In the second case, where the temperature reached 105° F., the cause of death, as proved by an autopsy, was extension of membrane. In the third case, where the temperature reached this point, the physical signs indicated a broncho-pneumonia. In eleven instances the temperature was 104° F., and the cause of death was as follows:— Broncho-pneumonia, 6; sepsis, 1; extension of membrane, 4. In four cases the clinical diagnosis was verified by an autopsy.

CASTS OF THE TRACHEA AND BRONCHI.

In one instance, where death was the result of broncho-pneumonia, there was membrane on the upper part of the œsophagus, but a stained section failed to reveal the presence of the specific organism of diphtheria. Case numbered 107, in the table, is of special interest, from the fact that at no time was there any membrane seen in the throat. When the patient was admitted he had a moderate amount of dyspnoea, which gradually increased during the following twenty-four hours, at the end of which time intubation was done. The tube remained in the larynx about one minute, when, during a violent fit of coughing, it was expelled, together with a cast of the trachea and right and left primary bronchus. After this the patient was comparatively comfortable for eighteeen hours, but at the end of this time the dyspnoea became urgent, and tracheotomy was about to be performed, when a severe paroxysm of coughing caused the expulsion of the second cast. The relief was so marked that no operative interference was demanded. The physical signs justified a diagnosis of broncho-pneumonia, with probable extension of membrane into the smaller bronchi. The accompanying illustration gives a good idea of the appearance of these casts. The one on the right was the first one expelled. The patient improved for a few days, but the process in the lungs continued to increase, and he died the tenth day after his admission to the hospital. At the autopsy the tonsils and pharynx were found to be hyperaemic, streaks of membrane were seen in the larynx and trachea; there was broncho-pneumonia of each lung, tuberculosis of the right upper lobe, with a small cavity and a fresh process. The kidneys were injected and cloudy. There was an abundant growth of streptococci in cultures taken from these organs. The remaining 105 cases had a temperature, ranging from normal to 103° F., which would seem to prove the correctness of the statement that a high temperature in diphtheria is of no very great prognostic value. Case 30 is of interest, from its great rarity. The patient, a child four years old, had been ill three days when admitted. There was moderate prostration, marked glandular enlargement and septic odor. On the tonsils there were large patches of necrotic membrane. No nausea, nor vomiting; temperature, 101°; pulse, 140. The patient

failed rapidly, and died the fourth day after entrance. At the autopsy diphtheritic membrane was found in the stomach. This membrane, which was thick, greenish brown in color, and gangrenous in appearance, extended from the cardiac orifice to the pyloric. The wall of the stomach was thickened. Stained sections showed the presence of the bacilli of diphtheria. Why such an extensive process in the stomach should not have caused nausea and vomiting cannot be explained.

Albuminuria is quite a constant symptom in diphtheria, and, as a rule, it appears early in the course of the attack, generally during the first week. The presence of albumin, if the amount is not large, is not a symptom of any very great gravity. In no case was there any indication of serious disease of the kidneys. Suppression of urine did not occur. In sixty-eight cases it was impossible to obtain a specimen of the urine for analysis, either from the severity of the illness or on account of the age of the patient. In one case one-fourth of one per cent. of albumin was found in the urine; in seven, one-eighth of one per cent.; in nine, one-tenth of one per cent.; a trace in six cases; in seven a slight trace; a very slight trace in one; the slightest possible trace in five; and in seven instances no albumin was found.

The area of cardiac dulness was found to be increased in seven instances, and in nearly every case there was a mitral systolic murmur detected. A full and complete analysis of the heart complications, occurring in diphtheria, will be found in the paper by Dr. C. M. Hibbard.

Membrane was found on the tonsils alone, ten times; the tonsils and uvula, thirty-three times; the tonsils, palate and uvula, thirteen times. There were fifty-one laryngeal cases. In all of the operative cases, except one, intubation was done. In two of these cases intubation did not relieve the stenosis, and, therefore, tracheotomy was done. In one case the initial operation was tracheotomy. Intubation in every case, except in the two just mentioned, relieved the laryngeal stenosis, but the patients died from broncho-pneumonia, or from extension of the membrane into the smaller bronchi, or from sepsis, and in a few instances from cardiac

failure. In no instance could death be attributed to a failure to relieve the laryngeal stenosis or to the operation. In the three cases in which tracheotomy was done, death was due to extension of membrane in two, and broncho-pneumonia in one. Where there was an autopsy, in no instance, in the intubation cases, was there the slightest indication that tracheotomy would have been the better operation; in fact, in many of the cases the condition of the patient was such that if the latter operation had been performed death would have occurred on the table. A careful consideration of the course of the cases, the manner of death, and the results of the autopsies, justifies the conclusion, that in children, in the vast majority of cases, intubation is the better operation. In adults tracheotomy is to be preferred.

There was marked septic odor in seventy-seven cases. The reason why a septic odor was not noticed in more instances is due to the fact that death occurred so early in the course of the disease that this symptom did not become apparent. Enlargement of the cervical glands was noticed in only a comparatively small number of cases, for a similar reason. A discharge from the ear was observed seven times, but this number does not give an accurate idea of the frequency of the invasion of the middle ear in diphtheria, as the results of autopsies prove. In quite a number of cases where there had been no symptom referable to the ear before death, at the autopsy membrane was found in the middle ear. It cannot be said that this was due to nasal irrigation, for in this series of cases nasal irrigation was not used. It is interesting to note that where there was a profuse nasal discharge, in nearly every instance, at the autopsy membrane was found in the ear.

The cause of death, verified by autopsy in seventy-one cases, was as follows: extension of membrane, thirty-nine instances; broncho-pneumonia, twenty-nine; sepsis, twenty-nine; cardiac complications, nineteen; abscess of the lung, two; tuberculosis, two; thrombi of the lateral sinus, one. It will be seen from this, that of the 121 fatal cases, in only thirty-nine instances was death caused by extension of membrane. Sepsis is the direct and immediate result of diphtheritic infection, and a similar remark is true regarding the

cardiac manifestations; but broncho-pneumonia must be considered a complication, and not an essential part of the process.

The average duration of illness before entrance to the hospital is recorded as about two and one-half days, but, judging from the condition of the patients, it is safe to presume that many of them had been ill a much longer time. Twenty-eight died within twenty-four hours of admission, or about twenty-two per cent. The average length of time in hospital before death occurred was about six days. Two patients were in hospital forty-one days. In one case, at the autopsy, the heart was found to be hypertrophied, the lungs oedematous and congested; there was double otitis media. The clinical symptoms just before death were those of cardiac paralysis. In the case of the other patient, who died forty-one days after admission, the cause of death was cardiac failure from a clinical point of view. There was no autopsy. At the end of thirty-three days cardiac failure caused the death of one patient, and one at the end of twenty-eight days. Broncho-pneumonia had a fatal ending, on an average, in about nine days. The average length of time, before death supervened in the septic cases, was about five days. Extension of membrane caused death in an average of about two days.

Of the intubation cases sixteen died within twenty-four hours of entrance; seven within two days; three within three days; fourteen over three days and less than fourteen; one case died in seventeen days and another in twenty-seven days. The cause of death in these last two cases was broncho-pneumonia. The intubation and tracheotomy cases died, one in eight days, the other in fourteen days; the cause of death in each instance being broncho-pneumonia. The tracheotomy case, an adult, died in two days; the cause of death being extension of membrane. It was noticed in all of the operative cases, when the tube was lined with a tough tenaceous muco-purulent secretion, not sufficient in amount to occlude it however, that death was imminent. No case in which this condition occurred recovered. Broncho-pneumonia after the laryngeal symptoms have been relieved by operation is a very frequent cause of death, and is an important factor in increasing the death-rate.

Tabular Statement of the Clinical History of 121 Fatal Cases of Diphtheria.

Number.	Age in years.	Sex.	Pulse.		Maximum Temperature.	Amount of Albumin.	Heart.		Membrane.			Nasal discharge.	Laryngeal.	Septic odor.	Glands.	Ears.	Duration at time of Entrance.	Number of days in Hospital.	Cause of Death.	Remarks.
			Maximum Rate.	Regular.			Size.	Murmur.	Tonsils.	Palate.	Uvula.									
1	2	M.	175	+	102°	?	N.	....	?	....	....	....	+	....	....	.....	?	2 days	Extension of Membrane.	Autopsy.
2	6	M.	150	+	101°	?	?	....	....	....	...	..	+	....	....	.....	4 days	1 day	Extension of Membrane.	
3	2	F.	160	+	99°	?	N.	....	+	...	....	....	....	....	...	.....	2 days	5 days	Broncho-Pneumonia.	
4	2	F.	140	+	101°	0	N.	....	....	....	....	....	+	....	....	.....	1 day	3 days	Extension of Membrane.	
5	1	F.	140	+	103°	?	N.	....	+	....	....	....	+	....	....	.....	2 days	2 days	Extension of Membrane.	Autopsy.
6	2	M.	160	+	101°	?	N.	....	+	....	....	....	....	....	....	. .....	3 days	4 days	Extension of Membrane.	Autopsy.
7	1	F.	140	+	101°	?	N.	....	....	....	....	+	....	....	....	Discharge from right ear	?	15 days	Broncho-Pneumonia.	Autopsy.
8	5	F.	140	....	100°	$\frac{1}{10}$ of 1 per cent.	N.	....	+	....	....	+	....	+	....	.....	4 days	1 day	Extension of Membrane.	
9	7	F.	110	+	97°	?	N.	....	....	....	....	....	+	....	....	.....	2 days	$\frac{1}{2}$ day	Extension of Membrane.	
10	9	M.	120	+	101°	$\frac{1}{10}$ of 1 per cent.	N.	....	+	....	....	....	....	+	....	.....	7 days	9 days	Sepsis.	
11	$\frac{3}{4}$	M.	160	+	97°	?	N.	....	....	....	....	+	+	....	....	.....	2 days	5 days	Broncho-Pneumonia.	Autopsy.

Tabular Statement. — *Continued.*

Number.	Age in Years.	Sex.	Pulse. Maximum Rate.	Pulse. Regular.	Maximum Temperature.	Amount of Albumin.	Heart. Size.	Heart. Murmur.	Membrane. Tonsils.	Membrane. Palate.	Membrane. Uvula.	Nasal discharge.	Laryngeal.	Septic odor.	Glands.	Ears.	Duration at time of Entrance.	Number of days in Hospital.	Cause of Death.	Remarks.
12	1½	M.	160	+	98.5°	?	N.	....	....	....	....	+	+	....	....	.....	2 days	12 days	Sepsis.	Autopsy.
13	5	M.	130	.. .	101°	Slight trace	Increased	M.	+	....	....	....	....	....	....	.....	3 days	14 days	Cardiac Failure.	Autopsy.
14	7	F.	150	+	104°	?	N.	....	....	....	....	+	+	....	....	.....	?	4 days	Broncho-Pneumonia	Autopsy.
15	3	M.	130	....	102°	Slightest possible trace	N.	M.	+	....	....	....	+	....	...	.....	?	28 days	Cardiac Failure.	Autopsy. Diphtheria of Œsophagus?
16	1½	M.	160	+	105°	⅛ of 1 per cent.	N.	....	....	....	....	+	....	....	....	.....	2 days	30 days	Sepsis.	Autopsy.
17	5	M.	135	+	101°	0	N.	....	+	....	....	+	...	+	....	.....	1 day	5 days	Extension of Membrane.	Autopsy.
18	¾	M.	140	....	102°	?	N.	....	....	....	....	+	....	+	....	.....	?	8 days	Broncho-Pneumonia.	Autopsy.
19	3	M.	140	+	100°	?	N.	....	....	....	....	....	+	....	....	.....	5 days	11 days	Sepsis.	Autopsy.
20	59	M.	130	....	103°	?	?	....	+	+	+	+	+	+	+	.....	3 days	1 day	Extension of Membrane.	
21	1	M.	140	....	99°	?	N.	....	+	....	....	+	....	+	....	.....	?	2 days	Thrombi of Lateral Sinus.	Autopsy.
22	19/12	M.	170	+	102°	?	N.	....	....	....	..	....	+	....	....	.....	1 day	10 days	Broncho-Pneumonia.	Autopsy.

23	5	M.	130	+	101°	?	N.	....	+	+	+	+	....	+	+	.....	4 days	1 day	Cardiac Failure and Sepsis.	Autopsy.
24	1½	M.	135	+	101°	?	N.	....	+	....	+	+	....	+	+	.....	4 days	12 days	Cardiac Failure.	
25	3	F.	160	+	101°	?	N.	....	....	....	....	+	+	..	....	.....	?	6 days	Broncho-Pneumonia.	
26	28	M.	100	+	104°	?	N.	....	+	....	....	+	....	+	....	.....	7 days	1 day	Extension of Membrane.	
27	1½	M.	160	+	98.5°	?	N.	....	....	....	....	....	+	...	....	.....	?	8 days	Broncho-Pneumonia.	
28	5	F.	180	+	104°	Trace	N.	....	+	....	....	...	+	+	+	.....	3 days	4 days	Broncho-Pneumonia.	
29	2	M.	170	+	100°	?	N.	....	+	....	....	....	+	....	....	.....	4 days	1 day	Extension of Membrane.	Autopsy. Diphtheria of Stomach
30	4	F.	120	+	101°	Slight trace	N.	....	+	+	+	+	....	+	+	.....	3 days	4 days	Broncho-Pneu. and Sepsis.	Autopsy.
31	2½	F.	135	+	98.5°	0	N.	....	+	....	+	+	....	+	+	.....	3 days	5 days	Sepsis and Cardiac Failure.	
32	3	M.	120	+	100°	?	N.	....	+	....	....	...	+	....	....	.....	?	2 days	Broncho-Pneumonia.	Autopsy.
33	7	F.	140	+	102°	Slightest possible trace	N.	....	+	....	....	+	+	+	+	.....	3 days	4 days	Extension of Membrane.	Autopsy.
34	1½	F.	140	+	101°	?	N.	....	+	....	....	+	....	+	+	.....	?	1 day	Extension of Membrane and Sepsis.	Autopsy.
35	5/12	M.	140	+	101°	?	N.	....	+	....	....	....	+	....	....	.....	?	1 day	Tuberculosis.	Autopsy.
36	5	F.	120	+	98.5°	?	N.	....	+	....	....	+	....	+	+	.....	3 days	1 day	Sepsis.	
37	5	M.	130	+	103°	?	N.	....	+	....	....	+	....	....	....	.....	3 days	12 days	Broncho-Pneumonia.	
38	35	M.	110	+	101°	Slight trace	N.	....	+	....	....	+	....	+	+	.....	3 days	3 days	Extension of Membrane.	Autopsy.

Tabular Statement. — *Continued.*

Number.	Age in years.	Sex.	Pulse. Maximum Rate.	Pulse. Regular.	Maximum Temperature.	Amount of Albumin.	Heart. Size.	Heart. Murmur.	Membrane. Tonsils.	Membrane. Palate.	Membrane. Uvula.	Nasal discharge.	Laryngeal.	Septic odor.	Glands.	Ears.	Duration at time of Entrance.	Number of days in Hospital.	Cause of Death.	Remarks.
39	2½	M.	170	....	103°	?	N.	....	+	....	....	....	+	....	....	.....	2 days	12 days	Broncho-Pneumonia.	
40	4	M.	150	+	103°	0	N.	M.	+	....	+	+	+	....	....	.....	?	5 days	Broncho-Pneumonia.	
41	2	M.	140	+	100°	?	N.	....	+	....	....	+	....	+	+	.....	?	1 day	Sepsis.	
42	5	M.	160	+	103°	?	.....	M.	+	....	+	+	....	+	+	.....	4 days	1 day	Extension of Membrane.	Autopsy.
43	5	F.	120	....	98.5°	Slight trace	N.	M.	+	....	+	+	....	+	+	.....	?	2 days	Sepsis.	
44	3	M.	150	+	102°	Slight trace	N.	....	+	....	....	....	+	....	....	Discharge from right ear	2 days	27 days	Broncho-Pneumonia.	
45	2	F.	150	+	102°	Very slight trace	N.	....	...	....	....	....	+	+	+	.....	2 days	9 days	Abscess of Lung.	Autopsy.
46	2	M.	160	+	98.5°	0	N.	....	....	...	....	+	....	....	....	Discharge from ears	1 day	34 days	Broncho-Pneumonia.	Autopsy.
47	1½	M.	140	+	101°	?	N.	....	....	....	....	....	+	+	+	.....	2 days	13 days	Broncho-Pneumonia and Tuberculosis.	Autopsy.
48	2½	M.	140	+	106°	$\frac{1}{16}$ of 1 per cent.	N.	M.	...	....	....	+	....	+	+	Discharge from ears	1 day	14 days	Broncho-Pneumonia.	
49	2	F.	130	+	101°	?	?	....	+	....	+	+	....	+	+	.....	3 days	4 days	Sepsis.	Diphtheria of Vulva.

50	14	M.	110	....	101°	$\frac{1}{8}$ of 1 per cent.	?	....	+	+	+	+	....	+	+	.....	7 days	8 days	Cardiac failure.	
51	$3\frac{4}{12}$	M.	150	....	99°	?	N.	....	....	....	....	....	+	....	....	.....	4 days	1 day	Broncho-Pneumonia.	Autopsy.
52	33	F.	120	....	101°	?	?	....	+	+	+	+	....	+	+	.....	?	1 day	Sepsis.	Autopsy.
53	10	F.	130	+	102°	Slight trace	N.	....	+	....	+	+	....	+	+	.....	7 days	4 days	Sepsis.	
54	3	M.	120	+	102°	?	?	....	....	....	....	+	+	....	....	.....	3 days	1 day	Extension of Membrane.	Autopsy.
55	1	M.	130	+	100°	?	N.	....	+	+	....	+	....	+	+	.....	?	1 day	Sepsis.	
56	4	F.	140	+	102°	?	N.	M.	+	+	+	+	+	+	+	.....	2 days	1 day	Extension of Membrane.	
57	5	F.	120	....	101°	0	N	M.	+	+	+	+	....	+	+	.....	?	8 days	Cardiac Failure.	
58	6	M.	160	+	101°	$\frac{1}{8}$ of 1 per cent.	N.	M.	+	+	+	+	...	+	x	.....	2 days	41 days	Cardiac Failure.	Autopsy.
59	2	M.	160	....	102°	?	.....	....	+	....	....	+	....	....	....	.....	2 days	1 day	Broncho-Pneumonia.	Autopsy.
60	8	M.	130	....	99°	$\frac{1}{8}$ of 1 per cent.	N.	M.	+	....	....	+	....	+	+	.....	9 days	13 days	Cardiac Complication.	Autopsy.
61	$6\frac{1}{2}$	M.	130	....	100.5°	$\frac{1}{16}$ of 1 per cent.	.....	....	+	....	+	+	....	+	+	.....	1 day	9 days	Sepsis.	Autopsy.
62	5	F.	150	+	98.5°	$\frac{1}{8}$ of 1 per cent.	N.	M.	+	....	....	+	....	....	....	Discharge from ears	?	21 days	Cardiac Thrombi.	Autopsy.
63	9	M.	150	....	101°	$\frac{1}{8}$ of 1 per cent.	N.	....	+	....	+	+	....	+	+	.....	5 days	33 days	Cardiac Complication.	
64	4	F.	100	....	101°	?	N.	....	+	+	+	+	....	+	+	.....	5 days	1 day	Sepsis.	Autopsy.
65	2	F.	140	....	98.5°	?	N.	....	+	....	+	+	....	+	+	.....	8 days	3 days	Sepsis.	
66	2	M.	130	....	100°	?	.....	....	+	....	+	+	....	+	+	.....	5 days	1 day	Extension of Membrane.	Autopsy.
67	9	F.	120	....	101°	?	N.	....	+	...	+	+	....	+	+	.....	4 days	1 day	Extension of Membrane.	Autopsy.

Tabular Statement. — *Continued.*

Number.	Age in Years.	Sex.	Pulse. Maximum Rate.	Pulse. Regular.	Maximum Temperature.	Amount of Albumin.	Heart. Size.	Heart. Murmur.	Membrane. Tonsils.	Membrane. Palate.	Membrane. Uvula.	Nasal discharge.	Laryngeal.	Septic odor.	Glands.	Ears.	Duration at time of Entrance.	Number of days in Hospital.	Cause of Death.	Remarks.
68	2½	F.	120	+	100°	?	N.	M.	+	....	+	+	....	+	+	.....	3 days	6 days	Cardiac Thrombi Sepsis.	Autopsy.
69	4½	F.	150	+	103°	0	N.	....	+	+	+	+	....	+	+	.....	3 days	5 days	Broncho-Pneumonia.	Autopsy.
70	6	F.	130	+	98.5°	$\frac{1}{10}$ of 1 per cent.	N.	M.	+	....	+	+	....	+	+	.....	4 days	2 days	Sepsis.	
71	7	M.	110	+	100°	Slightest possible trace	N.	....	+	....	....	+	....	+	+	.....	2 days	3 days	Sepsis.	Autopsy.
72	2½	F.	130	+	102°	?	N.	....	+	....	....	+	+	+	+	.....	2 days	1 day	Extension of Membrane.	Autopsy.
73	2	F.	140	+	100°	?	N.	....	....	....	....	....	+	....	....	.....	3 days	1 day	Extension of Membrane.	Autopsy.
74	2	M.	150	+	103°	?	N.	....	....	....	....	....	+	....	....	.....	1 day	5 days	Broncho-Pneumonia.	Autopsy.
75	3½	M.	150	+	101°	Slightest possible trace	N.	....	....	....	....	....	+	+	+	.....	1 day	7 days	Sepsis	Autopsy.
76	3	M.	130	+	102°	0	N.	....	+	....	....	+	....	+	+	.....	1 day	3 days	Sepsis.	
77	6	F.	120	+	98.5°	?	N.	....	+	....	....	+	....	+	+	.....	7 days	1 day	Sepsis.	Autopsy.
78	6	M.	160	+	103°	?	N.	....	....	...	....	....	+	+	+	.....	2 days	2 days	Extension of Membrane.	Autopsy.

79	3	M.	130	....	101°	?	Increased	M.	+	....	....	+	....	+	+	.....	1 day	7 days	Cardiac Thrombi.	Autopsy.
80	$\frac{3}{3}$	M.	150	....	102°	0	N.	....	....	....	....	+	+	+	....	.....	1 day	1 day	Extension of Membrane.	Autopsy.
81	7	F.	130	....	102°	$\frac{1}{10}$ of 1 per cent.	N.	....	+	....	....	+	....	+	+	.....	4 days	3 days	Sepsis.	
82	64	F.	130	+	103°	$\frac{1}{10}$ of 1 per cent.	N.	....	+	....	....	....	....	+	+	.....	?	2 days	Extension of Membrane.	Autopsy.
83	$3\frac{1}{2}$	M.	180	+	104°	Slightest possible trace	N.	....	+	....	....	....	+	+	+	.....	?	3 days	Sepsis.	
84	3	M.	180	+	105°	0	N.	....	+	....	....	....	+	....	....	.....	days	7 days	Extension of Membrane.	Autopsy.
85	5	F.	170	+	102°	Slight trace	N.	....	+	....	....	....	....	+	+	.....	2 days	3 days	Sepsis.	Autopsy.
86	$\frac{10}{12}$	M.	150	+	100°	?	N.	....	+	....	...	+	....	....	+	.....	3 days	19 days	Broncho-Pneumonia.	
87	1	F.	160	+	107°	?	N.	....	+	....	....	+	+	+	+	.....	?	2 days	Extension of Membrane.	Autopsy.
88	3	F.	....	....	?	?	.....	....	....	....	....	+	+	+	+	.....	4 days	1 day	Extension of Membrane.	Autopsy.
89	6	M.	130	+	100°	0	Increased	M.	+	+	....	+	....	+	+	.....	1 day	10 days	Cardiac Complication.	Autopsy.
90	1	M.	180	+	104°	?	N.	....	+	....	....	....	+	....	....	.....	1 day	2 days	Broncho-Pneumonia.	
91	$5\frac{1}{2}$	F.	150	....	100.5°	$\frac{1}{8}$ of 1 per cent.	Increased	....	+	....	....	+	....	....	....	.....	2 days	7 days	Cardiac Complication.	
92	7	M.	130	....	100°	$\frac{1}{10}$ of 1 per cent.	Increased	M.	+	....	....	+	....	+	+	.....	3 days	41 days	Cardiac Complication.	
93	2	F.	160	+	104°	?	N.	....	+	....	....	....	+	+	....	.....	1 day	2 days	Extension of Membrane.	
94	2	M.	120	+	100°	?	N.	....	+	+	+	....	...	+	....	.....	2 days	5 days	Broncho-Pneumonia.	

Tabular Statement. — *Concluded.*

Number.	Age in Years.	Sex.	Pulse. Maximum Rate.	Pulse. Regular.	Maximum Temperature.	Amount of Albumin.	Heart. Size.	Heart. Murmur.	Membrane. Tonsils.	Membrane. Palate.	Membrane. Uvula.	Nasal discharge.	Laryngeal.	Septic odor.	Glands.	Ears.	Duration at time of Entrance.	Number of days in Hospital.	Cause of Death.	Remarks.
95	2	M.	180	+	104°	?	N.	....	+	....	....	....	+	+	+	.....	2 days	2 days	Extension of Membrane.	
96	2	M.	160	....	104°	?	N.	....	....	....	....	....	....	+	....	.....	2 days	1 day	Broncho-Pneumonia.	
97	¾	M.	150	+	98.5°	?	N.	....	....	....	....	+	....	....	....	.....	?	17 days	Broncho-Pneumonia.	Autopsy.
98	61	F.	110	+	98.5°	0	N.	....	+	....	...	....	....	+	+	.....	2 days	3 days	Extension of Membrane.	Autopsy.
99	4½	F.	160	+	103°	?	N.	....	....	....	....	....	+	+	....	.....	6 days	2 days	Extension of Membrane.	Autopsy. Diphtheria of Œsophagus?
100	1⅓	M.	170	+	104°	?	N.	....	....	....	....	+	....	....	....	.....	?	4 days	Broncho-Pneumonia.	Autopsy.
101	1½	F.	160	+	101°	?	N.	....	....	....	....	+	....	....	....	Discharge from ears	3 days	8 days	Broncho-Pneumonia.	
102	2	M.	130	+	102°	0	N.	....	+	...	....	+	....	+	....	Discharge from ears	2 days	32 days	Abscess of Lung	Autopsy.
103	7	F.	160	+	102°	?	N.	....	+	....	....	+	+	....	....	.....	?	1 day	Extension of Membrane.	Autopsy.
104	3	F.	160	....	100°	?	N.	....	....	....	....	....	+	....	....	.....	?	1 day	Extension of Membrane.	
105	2½	F.	140	+	98 5°	?	N.	....	+	+	+	....	....	+	+	.....	3 days	2 days	Sepsis and Tuberculosis.	Autopsy.

106	5	F.	180	+	102°	?	N.	....	+	....	....	....	+	+	+	.....	4 days	1 day	Extension of Membrane.	Autopsy.
107	30	M.	120	+	104°	$\frac{1}{4}$ of 1 per cent.	N.	....	....	....	....	....	+	+	....	.....	?	11 days	Extension of Membrane, Broncho-Pneu.	Autopsy.
108	4	M	140	+	99.5°	?	N.	....	....	....	....	....	+	....	....	.....	11 days	1 day	Cardiac Failure.	
109	4	F.	100	....	100°	$\frac{1}{10}$ of 1 per cent.	N.	....	+	....	...	+	....	+	+	.....	3 days	13 days	Cardiac Complication.	
110	4	M.	160	+	101°	0	N.	....	+	+	+	+	....	+	+	.....	14 days	3 days	Sepsis.	Autopsy.
111	6	M.	130	....	101°	?	Increased	M.	+	....	+	+	....	+	+	.....	5 days	10 days	Cardiac Complication.	Autopsy.
112	4	M.	150	+	101°	?	?	?	+	....	....	+	....	+	+	.....	2 days	8 days	Sepsis.	
113	4	F.	180	....	101°	?	N.	....	+	....	....	+	....	+	+	.....	?	4 days	Extension of Membrane.	Autopsy.
114	5	M.	150	+	101°	Trace	N.	....	+	....	....	....	....	+	+	.....	1 day	6 days	Sepsis.	
115	2	M.	160	+	101°	?	N.	....	+	....	....	+	+	....	+	.....	1 day	3 days	Extension of Membrane.	Autopsy.
116	$1\frac{1}{2}$	F.	170	....	105°	?	N.	....	....	....	....	+	+	+	+	.....	1 day	10 days	Broncho-Pneumonia.	
117	$1\frac{1}{2}$	M.	160	+	100°	?	N.	...	....	....	....	....	+	....	....	.....	1 day	1 day	Extension of Membrane.	Autopsy.
118	2	M.	170	+	103°	?	N.	....	+	....	....	+	+	+	....	.....	2 day	17 days	Broncho-Pneumonia.	
119	2	M.	140	+	101°	?	N.	....	+	....	....	+	....	+	+	.....	?	7 days	Sepsis.	
120	45	F.	140	+	104°	Trace	Increased	M.	+	....	+	....	....	+	+	.....	?	2 days	Extension of Membrane.	Autopsy.
121	1	F.	160	....	102°	?	N.	....	....	....	+	+	+	+	+	.....	4 days	1 day	Extension of Membrane.	Autopsy.

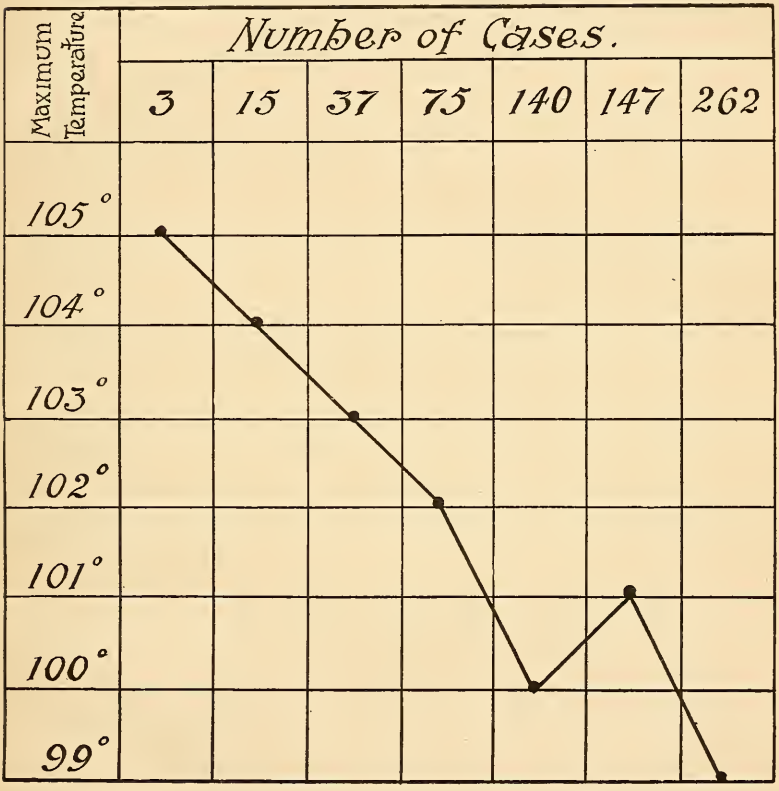
In the study of the 679 non-fatal cases it was observed that the pulse-rate was uniformly high; that in only twenty-seven instances was it below ninety, and that in seventy-six cases it was below 100. It may be said that the majority of the patients were children, and therefore the pulse-rate would naturally be rapid, but this does not explain the fact that in nearly every instance in the case of adults the rate was above 100. A similar condition was observed in the fatal cases. A chart, showing the maximum rate of pulse, with the number of cases, is appended. It has been already stated that the temperature is not specially elevated in diphtheria and that when an elevation of temperature is observed it is due to some complication, generally broncho-pneumonia. A study of the accompanying chart, which gives the number of cases with the maximum temperature, shows that only three had a temperature of 105°; fifteen a temperature of 104°; thirty-seven a temperature of 103°. The remaining 624 patients had a temperature of 102° and below.

An analysis of these cases shows that 411 had membrane on the tonsils; 134 on the tonsils and in the nose; thirty-five on the tonsils and uvula; eighteen on the tonsils, uvula and in the nose; in the larynx, eleven; on the tonsils and in the larynx, twenty-one; on the tonsils, in the nose and in the larynx, nine; on the tonsils, palate, uvula and in the nose, ten; on the tonsils, palate and uvula, seven; in the nose, six; in the nose and larynx, six; on the tonsils, uvula and in the larynx, five; on the tonsils and palate, four; on the tonsils, palate and in the nose, one; and in the eyes alone, one. A septic odor was noticed in 263 cases. The cervical glands were enlarged in 262 cases. Ear symptoms were observed in thirty-seven instances. There were eight cases of diphtheria of the eye, due to an accidental inoculation, generally from the discharge from the nose. In no instance did the diphtheritic process itself cause the loss of an eye, but in one case an old keratitis was excited to such an extent as to cause the destruction of this organ.

There were thirty-eight operative cases, thirty-seven of which were intubations, and one tracheotomy. In many of the intubation cases the tube was inserted several times. A short history of the individual cases may be of interest.

Chart of the Maximum Rate of Pulse, in 679 Non-fatal Cases of Diphtheria.

Chart of the Maximum Temperature in 679 Non-fatal Cases of Diptheria.



Case I. — A girl, four years old. Intubed once. Tube coughed up at the end of forty-eight hours. Not re-intubed. Made a good recovery in fifteen days, as far as laryngeal symptoms were concerned, but she remained in hospital a long time, owing to the presence of the bacilli of diphtheria in the throat.

Case II. — A boy, fourteen months old, coughed up the tube seven times. The tube was finally removed three days after the last insertion. The child wore the tube nineteen days. When he was discharged from the hospital his voice was natural in tone.

Case III. — A boy, four years old. Intubed on admission, and the tube extracted on the fourth day. No complications. Discharged well on the fourteenth day.

Case IV. — A boy, seven years old. Intubed on entrance. Tube extracted on the sixth day. Recovered from laryngeal symptoms in fifteen days. Broncho-pneumonia occurred as a complication. Discharged well.

Case V. — A boy, eleven years old. Intubed on entrance. Tube extracted on the fifth day. No complications.

Case VI. — A boy, six years old, intubed on entrance; tube extracted on the fifth day; re-intubed in two hours; tube extracted in three days; re-intubed in three hours; tube extracted the seventh day. No complications. Discharged well in twenty days.

Case VII. — A boy, age seven years. Steam was tried at first, but in a few hours the substernal retraction and the cyanosis were so marked that the boy was intubed four hours after entrance, with complete relief. He coughed up the tube at the end of twenty-four hours. Dyspnoea did not supervene. Discharged well in ten days.

Case VIII. — A boy, age two years, was intubed a few hours after entrance. The laryngeal symptoms, which were not marked on entrance, became very urgent in a few hours, and an intubation was done, with complete relief. The patient coughed up the tube on the third day. He had no further trouble, and was discharged well on the tenth day after entrance.

Case IX. — A girl, six years of age, was intubed on entrance. She coughed up the tube the next day, and was

immediately re-intubed. The tube was again coughed up in twenty-four hours and she was immediately re-intubed. On the eighth day, after the first intubation, the tube was extracted; but the laryngeal symptoms became so urgent shortly after the extraction that re-intubation was necessary. On the sixth day after the last intubation she coughed up the tube. There was no recurrence of the laryngeal symptoms, and the patient was discharged well. In this case there was a complication of broncho-pneumonia.

Case X. — A girl, eleven years of age. She was intubed on entrance, and coughed up the tube the next day; was immediately re-intubed. She coughed up the tube a second time, in twenty-four hours, and had no further trouble. The patient was in the hospital fourteen days.

Case XI. — A girl, four years old. Intubed on entrance, and tube extracted on the sixth day. No return of laryngeal symptoms. Empyema was a complication in this case. Discharged well of diphtheria and relieved of empyema.

Case XII. — A boy, eight years old. The patient at time of entrance had marked laryngeal stenosis. Complete relief followed intubation. He coughed up the tube in about six hours, but he did not require re-intubation. He was discharged well in thirteen days.

Case XIII. — A girl, three years old, had a patch of membrane on each tonsil, but there were no laryngeal symptoms until the third day after entrance, when intubation became necessary. The tube was in the larynx five days. Recovery in fifteen days, without complications.

Case XIV. — A boy, six years old, was intubed on entrance; the tube was extracted on the third day, but a re-intubation became necessary in a few hours. The patient coughed up the tube in twenty-four hours. He was discharged well.

Case XV. — A boy, six years old, intubed on entrance. Tube extracted on the third day, but a re-intubation became necessary in ten hours. The tube was finally extracted on the third day after the second intubation, and the patient was discharged well in fourteen days.

Case XVI. — A baby, three months old. Admitted with diphtheritic membrane on tonsils, great substernal retraction

and marked cyanosis. Intubed at once; tube coughed up on the third day. There was no return of the laryngeal symptoms. Recovery complete.

Case XVII. — A boy, four years old, was admitted with measles. Ten days after entrance he manifested urgent laryngeal symptoms and was intubed. The tube was expelled during a fit of coughing at the end of forty-eight hours; he was immediately re-intubed. In this case the patient was intubed thirty-seven times; the tube was extracted nineteen times, and he coughed it up eighteen times. The child had the tube in the larynx in all about 146 days. In several instances, before the tube was finally removed, there would be intervals of four or five days when he could breathe without it. When the boy was discharged his voice was natural in tone, his general condition was fairly good; there was no indication of any disease of the larynx.

Case XVIII. — A boy, two years old, with marked substernal retraction and cyanosis. Intubed on entrance. Coughed up the tube on the fourth day. No return of laryngeal symptoms. He made a rapid recovery.

Case XIX. — A girl, four years old. Admitted with marked laryngeal stenosis. She was intubed at once, coughed up the tube in twenty-four hours; no return of the laryngeal symptoms. She was discharged well in fifteen days.

Case XX. — A girl, six years of age. She was very cyanotic at time of entrance; had great substernal and supra-clavicular retraction. The pulse was feeble, and the patient was in a state of collapse. Intubed at once with complete relief of the laryngeal symptoms. After the tube had been in place a short time the symptoms of laryngeal stenosis returned; the tube was immediately removed, and the patient in a few moments coughed up a large piece of membrane. Relief was complete. The patient made a good recovery and was discharged well in eighteen days. No complications.

Case XXI. — A boy, six years old. Admitted with laryngeal symptoms of great severity. Intubed on entrance, and tube extracted in twenty-four hours. No return of laryngeal symptoms. In this case there was the complication of broncho-pneumonia. Discharged well in thirty-six days.

Case XXII. — A girl, nine years of age. Intubed on entrance; tube extracted on third day; re-intubed in ten hours; tube extracted again on the the third day; re-intubed in eight hours; tube finally extracted on the third day after the last intubation. Discharged well in twenty-four days.

Case XXIII. — A girl, three years old. Patient was cyanotic; had marked substernal retraction; was almost pulseless. Intubed at once. She coughed up the tube on the fourth day. There was no return of the laryngeal symptoms. Recovery was complete in fourteen days.

Case XXIV. — A girl, two years old. Slight laryngeal symptons at time of admission. At the end of twenty-four hours there was marked substernal and supra-clavicular retraction. Intubation was done. The tube was coughed up on the third day. The patient was well in fifteen days.

Case XXV. — A boy, two years old. Intubed, on entrance; tube extracted on fourth day on account of plugging and immediately returned; extracted on the sixth day. On the sixteenth day after the last extraction the laryngeal symptoms returned with such violence that intubation was done. On the third day after the last intubation the patient coughed up the tube and was immediately re-intubed. On the fifth and on the sixth day after the last intubation the tube was extracted and immediately returned on account of difficult breathing. In six days after the last intubation the tube was finally removed. From the seventeenth of one month to the twenty-fourth of the next this patient was intubed six times; had the tube extracted five times, and coughed it up once. He made a good recovery so far as the laryngeal symptoms are concerned, but had, as a complication, mastoiditis. He was discharged well in sixty-two days. The reason of his long stay in the hospital being the mastoiditis.

Case XXVI. — A boy, three years of age. Intubed on entrance; tube extracted on the sixth day. No recurrence of the laryngeal symptoms. Discharged well in sixteen days.

Case XXVII. — A girl, five years of age. Intubed on entrance; tube coughed up in nine hours. There was no return of the laryngeal symptoms for ten hours, when intubation became necessary. Seven hours later the patient

expelled the tube and a large piece of membrane, during a violent fit of coughing. She was immediately re-intubed, and on the third day coughed up the tube. No return of laryngeal symptoms. Discharged well in twelve days.

Case XXVIII. — A boy, four years old. Intubed on entrance; tube extracted on the fourth day. No return of laryngeal stenosis. Discharged well in seventeen days.

Case XXIX. — A girl, two years old. Intubed on entrance; coughed up the tube on the third day and was immediately re-intubed. Two days later coughed up the tube a second time; no return of laryngeal symptoms. Well in fourteen days.

Case XXX. — A boy, two and one-half years old. Laryngeal symptoms not marked on entrance; was put under steam for twenty-four hours, but at the end of this time the symptoms became so urgent that intubation was done. The relief was immediate and complete. The patient coughed up the tube three times and required re-intubation. On the fifth day after the first intubation the tube was finally coughed up. No return of stenosis. Broncho-pneumonia occurred as a complication. Patient was discharged well in thirty days.

Case XXXI. — A boy, four and one-half years old. Patient was very cyanotic and almost pulseless at time of entrance. While in the operating room the heart stopped beating, a tube was immediately introduced, artificial respiration commenced and hypodermic injections of brandy and ether given; after a short time natural respiration was induced and the cyanosis began to disappear; the child was breathing easily and naturally in half an hour. On the third day the tube was extracted, but it was necessary to re-introduce it in eight hours. The tube was extracted and introduced six times at intervals of four or five days. The tube was permanently removed at the end of thirty days. The patient made a good recovery, but was a long time in the hospital from the complication of broncho-pneumonia.

Case XXXII. — A boy, five years of age, intubed on entrance with very little relief. The larynx and trachea were wiped out with a feather with the result of removing a certain amount of membrane; he was then re-intubed with partial relief; in six hours the breathing became difficult and the tube

was removed and a feather again inserted into the trachea removing a certain amount of membrane. This was done five times in all with marked relief in each instance. The patient made a good recovery.

Case XXXIII. — A girl, two years old, intubed on entrance; tube extracted on the third day; re-intubed in eight hours; tube extracted a second time the third day after the last re-intubation; re-intubed in four hours; tube extracted next day; re-intubed in two hours; tube extracted; re-intubed immediately; tube finally extracted on the fourth day after the last re-intubation and the thirteenth day after admission. The child made a good recovery.

Case XXXIV. — A girl, two and one-half years old, intubed on entrance, coughed up the tube in an hour, and was immediately re-intubed; tube was extracted on the third day but re-intubation became necessary in four hours; the tube was finally extracted four days after the last re-intubation. The child made a good recovery and was discharged in twelve days, well.

Case XXXV.—A girl, four years old, laryngeal symptoms not urgent at time of entrance, but became so at the end of five hours. Intubed. Tube coughed up at the end of the third day. No recurrence of laryngeal symptoms. Discharged well in ten days.

Case XXXVI.—A girl, three and one-half years of age. Intubed twenty-four hours after entrance. Tube extracted on the third day. Re-intubed in nine hours. Tube finally extracted on the third day after the last intubation. Bronchopneumonia was a complication in this case. The patient was discharged well in thirty days. Recovery, so far as laryngeal symptoms were concerned, was completed in fifteen days.

Case XXXVII.—A girl, four years old. Intubed five hours after entrance, without relief. Tube was immediately extracted and found to be filled with membrane and mucus. The trachea was wiped out with a feather, after which the child coughed up several large pieces of membrane with marked relief. There was no recurrence of the laryngeal symptoms. The child was discharged well in twelve days.

The following tracheotomy case is worthy of mention from the severity of the symptoms and the critical condition of the

patient on entrance. The patient was a man twenty-five years of age. He had been ill three days. There was extreme prostration, great glandular enlargement and excessive œdema of the neck. The tonsils were very much enlarged, meeting in the median line. There were large patches of membrane on each tonsil, on the uvula and on the hard palate. There was intense hyperaemia of the mouth. Patches of necrotic membrane could be seen; the patient was cyanotic. A strong septic odor was noticed. Heart sounds were feeble. Temperature 99°. In short the patient was almost moribund; in fact when he was put in bed he stopped breathing. The trachea was immediately opened and artificial respiration was commenced. At the end of a few minutes he gasped and then commenced to breath naturally. He became conscious and said that he had felt no pain. On the fifth day the membrane commenced to be detached. He had five large doses of antitoxin at intervals of twenty hours, and was very freely stimulated. On the fifth day the tube was removed. On an examination of the throat the uvula which had been covered by the swelling of the tonsils could be seen. At no time did the temperature rise above 104°. The patient had a moderately severe attack of pneumonia. Œsophageal feeding was given owing to the inability of this patient to swallow, partly on account of paralysis and partly on account of the swelling of the fauces. At intervals the feeding caused vomiting, and nutrient enemata were tried. He made a slow recovery owing to post-diphtheritic paralysis, which was general. There is no doubt that this patient owes his life to tracheotomy, and also to antitoxin; the one would have been powerless without the other. Careful feeding and heroic stimulation were also very important factors in contributing to his recovery.

From the study of these cases of intubation the fact is evident that complete relief of the laryngeal symptoms occurred in nearly every instance, and that the period of convalescence was much shorter than would have been the case in the same number of tracheotomies. In case seventeen it may possibly be said that tracheotomy might have been the better operation, but a careful study of the attending symptoms pointed to intubation as giving the better chance of

saving the life of the patient, and hastening his ultimate recovery. In this case the liability to septic infection would have been very great, and this is one weighty argument in favor of intubation as compared with tracheotomy. Drs. R. W. Lovett and John C. Munro state in a paper entitled "A Consideration of the Results in 327 Cases of Tracheotomy," performed at the Boston City Hospital, from 1864 to 1887, that 232 died and 95 recovered, giving a percentage of recoveries of 29.05. In the same paper is a table compiled by them from German, British, French and American authors, embracing 21,853 cases, with a percentage of recoveries of twenty-eight. In the seventy-nine intubation cases, which form a part of these 800 cases of diphtheria, the percentage of recoveries is 46.8. In a previous report of 200 cases of intubation, by the writer, ninety-three recovered and 107 died. If these 279 cases of intubation with a percentage of recoveries of 46.5 are compared with the 327 cases of tracheotomy, to which allusion has just been made, it will be seen that in the former the percentage of recoveries was 46.5, while that of the latter was only 29.05. In an analysis of the cause of death in the 327 cases of tracheotomy it was found that of the 232 deaths, sepsis was responsible for sixty-two, or 26.7 per cent.; while of the 279 intubations, sepsis caused death in only twenty instances, giving a percentage of 13.4, as compared with 26.7 in the tracheotomy cases. From the nature of the disease in which tracheotomy is generally performed, the wound is specially liable to infection, not only from without but from within, and therefore any operation that will relieve the laryngeal stenosis, without solution of continuity of any of the tissues is to be preferred. It is not claimed that intubation is always to be done, in preference to tracheotomy, but it is claimed that in the majority of instances, intubation is the better operation. A comparison of the above statistics justifies this conclusion.

Of these 800 cases the urine was examined in 633. In 167 cases the urine was not obtained either on account of the age of the patient, or from the severity of the attack. The urine was analyzed usually on the day of admission, or as soon after as a specimen could be obtained, and then every four or five days. If the patient was very ill, or a trace of

albumin was found, the examination was made more frequently. The method of classifying the amount of albumin is the one at use in the hospital, and is purely arbitrary. From an analysis of these examinations, it was found that 42.3 per cent. of the cases did not have albumin; that 57.07 had the slightest possible trace; that 8.2 per cent. had a very slight trace; that a slight trace was found in 5.3 per cent.; that a trace was found in 4.4 per cent.; that 2.3 per cent. had a large trace; that one-tenth of 1 per cent. was found in 2.8 per cent. of the cases; that 4.1 per cent. had one-eighth of 1 per cent.; and that 1.1 per cent. had one-quarter of 1 per cent. of albumin. Albumin generally appeared within the first week, but occasionally during the second. The variation in the amount was considerable. For instance, in many of the cases, on one day there would be a large trace, and two days later only the slightest possible trace, and in some instances, none would be found by the ordinary tests. The variation in the amount of albumin is explained partly by the difference in the amount of urine secreted, and partly by the natural course of the disease. Œdema of the face was noticed four times out of the sixty-six cases, where there was a large amount of albumin. In no instance did complete suppression of the urine occur. A comparison was made in 615 cases as to the frequency of albuminuria in patients who had enlarged cervical glands. These, of course, were the cases in which there was generally a serious infection of the disease. It was found that albumin was absent in only twenty-nine per cent. of the 308 cases in which there was cervical adenitis, while in 57.7 per cent. albumin was absent in 307 patients who did not have this symptom.

A comparison of the results of the examination for albumin, and the bacteriological investigations, at the autopsy, of the heart's blood, kidneys, spleen and liver, did not develop anything of interest. In the fifty-one cases where the amount of albumin was one-tenth of one per cent. or more, fourteen of the patients had cardiac complications; six were laryngeal; three had suppurating glands; three had pneumonia; fourteen had a very severe infection and the remaining eleven, moderately severe attacks of diphtheria. It would seem from this that

albuminuria is usually due to the toxin of the disease and that the apparent mildness of the infection so far as the extent of the membrane is concerned is not a safe guide as to the effect of the toxin on the kidneys. It cannot be claimed that antitoxin is a factor in the causation of this symptom for the percentage of cases in which albumin was found is no greater than was found before the days of antitoxin.

The prognostic value of the presence of albumin in the urine varies with the amount found, but is of no very great significance. An analysis of the urinary examinations of 586 patients shows that 5.7 per cent. who had no albumin in the urine, died; that when there was the slightest possible trace three per cent. died; that the percentage of mortality when there was a very slight trace of albumin was 5.8; that when there was a slight trace the death-rate was 5.9 per cent.; that in the cases where there was a trace of albumin the per cent. was 7.2; that the rate of mortality where there was a large trace was 13.3 per cent.; that the death-rate was 50 per cent. when there was one-tenth of one per cent.; when there was one-eighth of one per cent. the rate was 30.8 per cent.; when there was one-fourth of one per cent. it was 15.9. In the seventy-one autopsies, in no instance was the condition of the kidneys such as to have materially contributed to the fatal issue.

Diphtheritic membrane on the skin, due to an accidental inoculation, generally with the discharge from the nose, was noticed six times. In no instance was the patient seriously inconvenienced by it. Two cases of diphtheria of the penis were noticed.

Case I. — The patient, four years of age on his admission had a profuse nasal discharge, cultures from which showed the presence of bacilli of diphtheria. Some little time after his admission there was pain and tenderness of the prepuce and some pain in micturition. On retracting the foreskin two small patches of membrane, diphtheritic in appearance, could be seen. Cultures were positive. These patches of membrane disappeared in a few days leaving ulcerated spots that healed in a short time. A Guinea pig, weighing 210 grammes was inoculated subcutaneously

with two loops of a pure culture of the bacilli of diphtheria from the penis of this patient. The pig was found dead in twenty-four hours. Autopsy of pig: Subcutaneous tissue around inoculation wound œdematous and haemorrhagic; slight increase of fluid in pleural and peritoneal cavities; adrenals enlarged and intensely hyperaemic. Smears from inoculation wound show many of the bacilli of diphtheria, free and enclosed in leucocytes. This child had not been circumcised. The source of infection in this case was without doubt the nasal discharge.

Case II. — A child, one year and ten months old, was admitted to the hospital, having been ill with diphtheria three days. On admission his condition was as follows: A well-developed and well-nourished child; no discharge from the nose. The throat was distinctly hyperaemic; no membrane was seen. There was sternal and clavicular retraction and marked cyanosis. The child was immediately intubed and given twenty c.c. of antitoxin. Cultures were positive. Two days after admission a small patch of diphtheritic membrane appeared on the inner aspect of the lower lip. Four days after admission, tube extracted. On this day it was noticed that the child's glans penis was red and œdematous. On the next day the swelling and redness had increased. Slight reddish secretion noticed, a culture from which showed the presence of the bacilli of diphtheria. No membrane was seen. Five days after the appearance of the œdema the condition of the glans penis was normal. Inoculation experiment was negative. In this case it is reasonable to suppose that the bacilli were carried from the patch of membrane in the mouth to the penis. This child had been circumcised.

In quite a number of instances cultures taken from the vulva have been found to be positive. In only a few instances, however, have there been patches of membrane of any considerable size. In these cases there has been a certain amount of discomfort on micturition, but apparently no severe pain.

The length of time after the disappearance of the membrane from the throat before two consecutive negative cultures from the throat and from the nose could be obtained, varied very considerably; in some instances being from forty-three

to forty-seven days, with an average of about seven days. It was noticed that in children with hypertrophied tonsils and adenoids, the bacilli of diphtheria persisted for a long time. No method of treatment was of any special advantage in these cases.

Antitoxin has been given in every case in large doses. If at the end of twelve hours there was not a marked improvement in the patient a second dose was given, and in some instances a third, a fourth, and also in extreme cases a fifth dose. The initial dose, as a rule, except in the case of very young children was twenty c.c., estimated approximately to contain about 1,000 units. The amount given was much larger than has generally been used, and the intervals between the doses were shorter than is usual. In no instance, however, was there the slightest indication of any injurious effect on the patient. On the other hand, the beneficial effect was very marked in the vast majority of instances. There is much greater danger of giving too small a dose of antitoxin than too large a dose. The difficulty of knowing just what amount of antitoxin should be administered is due to the fact that we do not know how much of the toxin of the disease is to be antagonized. In the case of Guinea pigs that are used for testing the serum, a certain definite amount of toxin is injected, and that is antagonized by a certain amount of the healing serum. In the case of human beings, ill of diphtheria, however, it is impossible to know the degree of toxicosis, and therefore it is better to err by giving large doses than to make the mistake of giving too small a dose. There is not the slightest evidence in a study of 2,772 cases of diphtheria treated by antitoxin that the healing serum in any instance caused any serious trouble to the patient. It is true that urticaria and arthralgia may give the patient a certain amount of annoyance, but the occurrence of these symptoms should not deter any one from the administration of the healing serum. From 1,000 to 2,000 units should be given as the initial dose, unless the patient is a very young child, and this dose should be repeated within twelve to twenty-four hours, unless there is a marked amelioration of the symptoms. Of course, it is important that the serum should contain the largest number of units in the smallest

amount of fluid possible, in order that a large quantity of fluid should not be injected at once. In many of the non-fatal cases, as has been before stated, four and five doses of antitoxin were given, with marked benefit to the patients. In fact there can be no doubt that these patients would have succumbed to the disease if it had not been for antitoxin.

Dr. Alexander McAlister, in a paper entitled "Serum Therapy in Diphtheria: its Present Status," published in the "Journal American Medical Association," 1897. Volume XXIX., No. 4, states that of more than 2,000,000 injections, in only five instances did the injections cause sudden death. It is very doubtful, however, if death was the direct and immediate result of the injections. It is very important that the healing serum should be given at the earliest possible stage of the disease, for it has been observed in the 2,772 cases of diphtheria treated at the South Department that the majority of the patients, who had been ill only one or two days before entrance, recovered; while of those who been ill five or six days a large number died.

The death-rate in these 2,772 cases was 13.9 per cent. If the moribund cases, of which there were ninety-eight, are eliminated it will bring the death-rate down to 10.8 per cent. From the condition of these moribund patients on admission it was perfectly evident that most of them must have been ill at least one week before entrance. This is a most convincing argument in favor of the early administration of antitoxin.

Alcoholic and cardiac stimulants have been very freely administered with marked benefit. Applications to the throat, as a rule, have not been made. Saline irrigation of the throat, while not affecting the course of the disease has contributed largely to the comfort of the patients. Irrigation with a weak solution of corrosive sublimate has been used somewhat frequently, but it did not seem to be of any special advantage in comparison with the saline irrigation.

From the study of these 800 cases of diphtheria, the following conclusions are justifiable:

First. That the pulse-rate in diphtheria is uniformly accelerated.

Second. That the temperature in this disease is not specially elevated.

Third. That in the laryngeal cases intubation is the operation of election.

Fourth. That albuminuria is quite a constant symptom in diphtheria.

Fifth. That the use of antitoxin has very materially reduced the death-rate of diphtheria.

II.

HEART COMPLICATIONS IN DIPHTHERIA.

By Cleon Melville Hibbard, A.M., M.D.,

First Assistant Resident Physician, South Department of The Boston City Hospital.

The following observations are the result of a study of 800 consecutive cases of diphtheria in the South Department of the Boston City Hospital:

Pulse rate. — Observations on the maximum rate were made in 798 cases, the results were as follows:

Rate.	Recovered.	Died.	Per cent. of mortality.
Less than 130	436	22	4.8
130	114	22	16.2
140	85	19	18.2
150	24	16	40.0
160	18	23	56.1
170	1	7	75.0
180 and higher	1	10	90.9

In over half of the cases the rate did not exceed 130 per minute, and the mortality among these was less than five per cent. As the rate increased so did the percentage of death. Less than half of those whose rate was 150 or over, recovered. In other words, a high pulse-rate of 150 or more is prognostic usually of a fatal result.

Bradycardia. — In twenty-three cases the pulse-rate was as low as sixty per minute on one or more occasions. Among the fourteen who were seventeen years of age or older there were no deaths, and only two had other cardiac symptoms. Of the six who were less than seven years there were four deaths from heart and one from lung disease. Of nine who were less than seventeen years all but one had had some other cardiac symptom.

Thus it appears that in diphtheria a transitory slow pulse in adults has no special significance; while in children, and particularly in young children, it is a symptom of cardiac trouble, often of a grave nature.

Irregularity of pulse. — This was noted in seventy cases of this series. But this number cannot be taken to represent the exact frequency, as some cases were doubtlessly not recorded. However, it can be safely said that at least ten per cent. of diphtheria cases have an irregular or an intermittent pulse some time during the course of the disease. It was observed generally in the severe cases of infection, and but six times in the mild attacks.

The time when it was first recognized varied anywhere from the day of admission to several weeks in the convalescence; often it was during the first few days that the patients were up, especially if they became fatigued. The duration lasted from a day to weeks. Excepting in the fatal cases, it usually disappeared in a few days if the patient remained quiet in bed.

The significance of this irregular pulse is shown by the fact that in over half of the cases where it was observed there were other heart symptoms as murmurs, or the patient died of cardiac trouble, as from dilatation and heart paralysis.

An irregular or intermittent pulse was often noticed several days before the appearance of the systolic murmur at the apex.

The frequency of this irregularity in the fatal cases of diphtheria is seen in the statement that it was noted in one-fourth of them, which is surely too low a percentage. The mortality among these seventy cases, with an irregular pulse, was thirty-one, or about 47 per cent.; in nineteen of the seventy cases there was also an intermittency with nine deaths.

The cause of this arrhythmia is most probably due to certain changes in the vagus nerve interfering with the innervation of the heart or to local changes in the cardiac ganglia or the myocardium.

No record was kept of irregularities in the volume of the pulse. However, it was often noticed when the rate was rhythmical; and such variations in the volume are surely as common as in the time.

A weak pulse was more frequent than an irregular one, and was of about the same clinical importance as to the prognosis and the treatment.

A reduplication of the heart's second sound was observed in six cases. A systolic murmur at the apex was heard in four of these. Three of these six cases died. There were doubtless other instances of a reduplication that were overlooked. Still, one must consider this as a symptom indicative of a possible serious result.

Cardiac murmurs. — All the murmurs heard in the children in this series were systolic in time, with the exception of three cases of chronic heart disease. The location was about equally divided between those heard loudest at the base and those loudest at the apex.

The basal murmurs, usually most distinct over the pulmonic area, were frequently heard on admission, continuing for a few days; or during convalescence, especially in anaemic patients.

A systolic murmur at the apex was noted fifty-seven times in this series. In another series of 252 cases where the hearts were examined almost daily a systolic murmur at the apex was heard in twenty-eight patients. In other words, a systolic murmur at the apex with an accentuated pulmonic second sound, and often with some enlargement of the cardiac dulness is seen in about ten per cent. of diphtheria cases during the course of the disease. The time when it first appeared in forty-four cases was as follows:

During	the	first	week	of	illness	.	.	.	.	9 cases.
"	"	second	"	"		.	.	.	.	2 "
"	"	third	"	"		.	.	.	.	9 "
"	"	fourth	"	"		.	.	.	.	5 "
"	"	fifth	"	"		.	.	.	.	2 "
"	"	ninth	"	"		.	.	.	.	1 "

The duration of this murmur varied from one day to several months. In twenty-four cases where the heart was under observation until the murmur disappeared the time was as follows:

Within one week	. . .	10 cases.
" two weeks	. . .	6 "
" three "	. . .	5 "
" four "	. . .	1 "
" five "	. . .	1 "
" eight "	. . .	1 "

There were fifteen cases in which the murmur was heard on discharge at the end of from five to sixteen weeks from when first observed, and in some of these cases it was heard two months after leaving the hospital.

The character of this murmur varied from a very soft blowing sound to a rough one. In some it could not be heard outside of the apex; in others it was transmitted into axilla or heard over the left back. In two cases it was musical. This character of the murmur appeared in one on the tenth day, and was still heard at the end of five months; the other on the thirtieth day, and disappeared in two weeks.

There is no special prognostic significance to an apical systolic murmur with an accentuated pulmonic second sound when the patient is kept quiet. The mortality among these cases having such a murmur was practically the same as for diphtheria cases in general. However, when there is associated with these signs, marked enlargement of the area of cardiac dulness, *i.e.* — in children as much as 2 cm. outside of the normal limit — the prognosis is usually fatal. In other words the significance of this murmur depends entirely on the nature of its cause.

The aetiology of this murmur in diphtheria is probably due to a variety of conditions; possibly, but rarely, to an endocarditis from the diphtheria bacillus;[1] but generally to a relative mitral insufficiency. This inadequacy is due in all probability to an insufficient contraction of the cardiac muscle, or to a dilatation of the ventricle owing to changes in the innervating nerve or the myocardium itself.

If the murmur is due to only a slight weakness of the heart muscle, the prognosis is usually good, since the murmur

[1] Dr. R. M. Pearce, in his Bacteriological Report, mentions a case of acute endocarditis in a patient who died of diphtheria, measles and pneumonia, where the origin may possibly have been from the Klebs-Loeffler bacillus. See page 95 of this report.

generally disappears after a few weeks, providing the patient is kept quiet in bed. If the cause is from a dilatation of the ventricle the outlook is less favorable, and depends upon the degree of the dilatation.

To sum up, — The great importance of this murmur is, that it informs the physician that there are some changes in the heart's machinery, and that no extra strain should be put upon that organ; and it again informs him of the necessity of frequently determining the area of cardiac dulness in these patients to ascertain if there is any dilatation.

The treatment of these cases was, first of all, *rest in bed;* the patient was kept as quiet as possible in a recumbent position, usually, until the murmur had disappeared for a week. Then the child was allowed to sit up for a short while. The time of being up was extended if the murmur did not reappear, otherwise the child returned to bed. If the murmur persisted at the end of six or eight weeks and there was no dilatation, and the heart's action was regular, the patient was permitted to sit up an hour or less, daily, for a week. At the end of this time, there being no untoward symptoms, the time was gradually lengthened until the patient was up for the greater part of the day. In one instance it was four months before the patient could be up all day without ill effect on the heart. The medicinal treatment consisted usually in strychnia, alcohol, digitalis group and occasionally caffein.

A discussion of twenty-two fatal cases of diphtheria, where the cause of death was chiefly due to some cardiac trouble, as dilatation, thrombi, paralysis, etc., is not without interest. Below is a brief clinical record of these cases, with a report of the post-mortem examination, from the records of the Pathological Laboratory of the Hospital, where these were obtained. In eight cases,[1] the pneumogastric nerve was examined by Dr. J. J. Thomas. As he has kindly given me the result of his findings,[2] these are also added. He used Marchi's method of staining.

No. 59.—Boy, aged five years. Had measles and scarlatina. Admitted July 17, after an illness of two days, with a moderate severe attack of diphtheria. There was

[1] Nos. 59, 63, 79, 105, 325, 331, 363 and 534.

[2] For a full and detailed description of this work see page 52 of this report.

nothing unusual in the course of the disease during the first week save that he was somewhat languid. On the fourteenth day the pulse was 130, irregular and weak. Cardiac dulness extended 1.5 cm. outside nipple line, and 4 cm. to right of median line. There was a bruit de galop heard all over precordia, loudest at apex. The first sound over the pulmonic area was sharp and valvular. Vomited twice during the day; had a restless night. Next day had a partial collapse. Heart dulness 1 cm. further to both right and left, the apex beat in sixth space. A systolic murmur heard at apex. Pulse weak, irregular and intermittent. Complained of pain in right iliac region. No note of any paralysis. Died on the seventeenth day.

Post-mortem examination. Heart enlarged; weighed 120 gms. All cavities much dilated and filled with post-mortem clots. Auricular-ventricular valves, especially the mitral, were dilated. Heart muscle yellowish and opaque. Congestion of lungs, liver, spleen and kidneys.

Pneumogastric nerve showed marked and extensive degeneration of a large proportion of the fibres with considerable fatty change. Section of the floor of the fourth ventricle of the brain showed a moderate degeneration of the nerve fibres, while the cells were normal.

No. 63.— Boy, aged three years. Had measles three months prior to admission. Entered hospital March 5, with tonsillar and laryngeal diphtheria. Child improved rapidly, and went home in eight days. Re-admitted in thirteen days on account of some laryngeal symptoms. Had then one-eighth of one per cent. of albumin with casts and fatty renal cells. Œdema of ankles. On the thirtieth day had a collapse, pulse which had varied between 110 and 130 was so rapid and weak that it could not be counted. A systolic murmur heard at apex. Died suddenly the same day. There was a nasal voice; he was rather dull and stupid during the last week.

Post-mortem examination. Heart enlarged, weight, 120 grammes. Valves and cavities normal. Slight bronchopneumonia and general acute lymphatic hyperplasia.

Pneumogastric nerve showed considerable numbers of degenerated fibres, with but little fat. Most of the fibres were, however, normal.

No. 79. — Boy, aged three years. Admitted March 31, after an illness of five days, with laryngeal diphtheria. He was intubed on entrance. The tube was removed twice, but had to be re-introduced at once. On the eleventh day in hospital coughed the intubation tube up and was dead in less than a minute. No note of any paralysis.

Post-mortem examination was practically negative save for slight hyperplasia of the lymph glands. Heart: weight, sixty-five grammes, normal.

Pneumogastric nerve showed marked degenerative changes of most of the fibres. There was considerable fat present in both the nerve sheath and the axis cylinder.

No. 105. — Boy, aged five years. Had measles. Admitted July 19 with diphtheria of two weeks standing; was in a very septic condition. Pulse was weak, 78. He failed rapidly, and died the next day. No note of any paralysis.

Post-mortem examination. There was diphtheritic pharyngitis, tonsillitis, glossitis; congestion of lungs, spleen and liver with ascites and hydrothorax. Heart enlarged, weight 140 grammes. Left ventricle dilated; both sides contained clotted blood. Both mitral and tricuspid valves seemed somewhat dilated.

Pneumogastric nerve had rather a slight degeneration of the fibres, and only a moderate number of them were affected.

No. 117. — Boy, aged twenty months. Admitted April 8 with diphtheria of nose and throat of four days continuance. Throat cleared up in four days. Pulse varied between 140 and 100. On the thirteenth day in the hospital he suddenly died. There was a profuse nasal discharge on the eleventh day. No post-mortem examination.

No. 171. — Girl, aged two and one-half years. Admitted April 21, with septic diphtheria of throat and nose after an illness of three days. She remained in a prostrated condition. Pulse varied from 110 to 130 and on the eighth day of illness fell to 80, weak in volume. Died on this day. No note of paralysis. No post-mortem examination.

No. 247. — Girl, aged five years. Had measles. Admitted May 8, with septic diphtheria of nose and fauces. On the third day pulse fell from 120 to 72; it had been irregular

from the first. Had a collapse on this day and died in seven hours. No record of paralysis. No post-mortem examination.

No. 284.— Boy, aged fourteen years. Admitted May 18, with a severe case of septic diphtheria of eight days duration. Albumin one-eighth of 1 per cent. Began to vomit on third day in hospital, and this vomiting persisted. He had a marked nasal voice and regurgitation. He was dull and lost weight from the first. Pulse was very weak; no murmur. He suddenly died on the fifteenth day of the disease. No post-mortem examination.

No. 316. — Girl, five years old. Admitted May 27, with a moderately severe attack of diphtheria. Pulse, 120, regular, and of good strength. On the fourth day pulse fell from 90 to 50 and was of poor volume. The child had been in a rather languid state since admission, would not sit up in bed. No paralyses were observed. She gradually failed and died on the eighth day in the hospital. No post-mortem examination.

No. 325. — Boy, aged six years. Admitted May 29, with pharyngeal and nasal diphtheria of two days continuance. During the first fortnight the throat cleared up. On admission, the heart area was normal, and a loud systolic murmur was heard at apex. Pulse varied between 120 and 70. The child took little interest in the affairs of the ward. The urine had a trace to one-eighth of 1 per cent. of albumin. There was paralysis of the palate. On the thirteenth day in the hospital the heart dulness had extended from 1 cm. to the right of sternum to 1 cm. to left of mammary line. Pulmonic second sound was accentuated. The second sound at the apex was reduplicated every ten or twelve beats. For a time the murmur disappeared. On the forty-first day the heart's dulness extended to 2 cm. outside of nipple line. There was a soft systolic murmur at the apex; the re-duplication was more constant. Died on forty-third day of his illness.

Post-mortem examination. Œdema, congestion and some atelectasis of lungs. Heart slightly enlarged; weight, 115 grammes. Some hypertrophy, possibly, of left side.

Pneumogastric nerve had a very slight degenerative process, only a few fibres were affected, and rarely a few fat drops. Unfortunately none of the heart muscle was saved.

No. 331. — Boy, eight years old. Admitted June 1, with diphtheritic pharyngitis and some laryngeal symptoms of eight days duration. On admission, heart sounds and area normal. Pulse regular, varied for ten days between 70 and 100. Five days later he was noticed to be quite dull. His color was pale. Heart sounds weak. Urine had one-eighth of 1 per cent. of albumin. Evidently losing weight. On the ninth day in the hospital there was a suggestion of a systolic murmur at the apex. Had a marked nasal voice. Two days later a faint murmur was heard. The first and second sound at the apex were of the same length. Occasionally there was a reduplication of the first or second sound. The action was irregular. Next day the radial pulse could not be felt. Heart beats were 134. Vomited some. Complained of pain in right knee and toe (the cause of this symptom was not evident). Patella reflexes diminished. Extremities cold. Lips cyanotic. The following day, the fifteenth of illness, two hours before death, heart rate was 200, and during inspiration would stop for three or four beats. A bruit de galop heard over the whole precordia.

Post-mortem examination. Heart enlarged, weight 155 grammes. Length from base to apex 13 cm.; transverse diameter 10.5 cm. All cavities distended with blood. In the auricular appendages there were delicately mottled grayish white clots. Tricuspid valve would almost admit the tips of four fingers, and the mitral three. The left ventricle greatly dilated, walls averaging 0.8 to 1 cm. in thickness.[1] Valve curtain normal. There was also atelectasis of left lung and sub-pleural ecchymoses.

Pneumogastric nerve had a moderately but diffuse degeneration of the fibres with little fatty change. In the medulla the nerve cells were normal, but the fibres were quite diffusely degenerated.

No. 363. — Boy, aged six and one-half years. Had measles, scarlatina, diphtheria and pertussis. Admitted June 10 with septic diphtheria of nose and throat, and was in a prostrated condition. He began to vomit on the third day

[1] The normal length is 7.04 cm.; breath, 7.44 and thickness, 0.86 for a child five to nine years old. (See Keating's Cyclopædia of the Diseases of Children. Vol. XI., p. 790.)

and later would retain nothing by mouth. Urine contained one-tenth of one per cent. of albumin. Child was restless, rolled and tossed about the bed. Heart action regular; no murmur was ever heard: pulse was weak; there was nasal regurgitation. During the last two days was semi-conscious. Died on the eleventh day of his sickness.

Post-mortem examination. Heart slightly enlarged; weight 105 grammes. Left ventricle slightly dilated; mitral valve readily admitted two fingers beyond the first joint. Wall from 0.5 to 1.2 cm. thick. Other valves normal. The rest of the examination showed a diphtheritic rhinitis and tonsillitis, and acute general lymphatic hyperplasia.

The pneumogastric nerve had a moderately extensive degeneration of the fibres, the majority of which showed the presence of fat.

No. 369. — Girl, aged five years. Had measles, diphtheria, pneumonia; and was just over scarlatina and chorea. The symptoms of the latter still persisted. Admitted June 12, after an illness of three days with diphtheria of nose and throat. The urine had one-eighth of 1 per cent. of albumin with some fat (post-scarlatina). Heart on admission was regular, and there was a loud systolic murmur at apex, which persisted until death. Pulse varied from 130 to 140. There was a nasal voice. Patient appeared to gain some during the first fortnight, then was at a stand-still until about three days before death, which was on the twenty-first day in the hospital. She died in a partial collapse, which lasted about twelve hours.

Post-mortem examination. Pericardial fluid slightly increased. Heart enlarged; weight, 115 grammes. Left auricular appendage contained an irregular, rather roughened, grayish opaque thrombus $1 \times 1 \times 2$ cm. In left ventricle, on the anterior wall, was a thrombus $1 \times 4 \times 5$ cm.; both sides of heart contained considerable clotted blood. Atelectasis of lungs with œdema and congestion. Chronic passive congestion of liver.

No. 377. — Boy, aged nine years. Had diphtheria and scarlet fever at six. Has always been excessively fat; weighed 120 pounds on admission, June 12. He had then a severe septic diphtheria of nose and throat of three days

continuance. Pulse was weak, and heart sounds were faint. Albumin one-eighth to one-fourth of 1 per cent. Began to vomit in a few days, and this continued during life with more or less persistency. On the fourteenth day cried out with pain, referred to cardiac region; this would last for eight or ten minutes. Had a marked nasal regurgitation and voice, and had also great difficulty in swallowing. Towards the end, retained no food by mouth. He failed gradually, and during the last three days was delirious. Frequent examinations of the heart showed only a feeble and irregular action, no murmurs. Area of dulness undetermined on account of excessive fat. Died on the thirty-eighth day of illness. No post-mortem examination.

No. 400. — Girl, aged two and one-half years. Admitted June 21, with septic nasal and faucial diphtheria with considerable prostration; sick three days. There were several ecchymoses on body. Pulse varied from 100 to 120, and gradually became weak. Circulation poor, lips cyanotic, extremities cold. Child was languid, took nourishment poorly. Failed gradually from the first, and rapidly during the last two days. Died in a collapse on the ninth day of sickness.

Post-mortem examination. Heart enlarged; weight, 75 grammes. In left ventricle, almost at apex, a yellowish, opaque, firm, rough thrombus 1½ cm. in diameter, attached by a small pedicle 2 cm. from apex to the intra-ventricular septum.

Besides this old clot, there were considerable elastic, transparent, pale post-mortem clots. On section, the thrombus appeared to be of a uniform consistency. Valves normal. Other findings. Diphtheritic tonsillitis and rhinitis.

Pneumogastric nerve showed rather extensive degeneration of the fibres, with but little fat. In the medulla there was a slight, acute degeneration of the fibres, while the cells were normal.

Section of the heart and thrombus showed a degeneration of the myocardium where the thrombus was attached.

No. 463. — Boy, aged three years. Admitted July 3, with diphtheria of the nose and throat. Had considerable prostration. Throat was clear within four days, and there were no

untoward symptoms until the fifth day, when the pulse fell to 50. Later in the day it was so weak it could not be counted. On the following day had a collapse, after which he was very restless. During the next day, heart rate 54. Cardiac dulness from nipple line to 1.5 cm. to right of sternum. His extremities were cold and clammy. Died on the eighth day of illness.

Post-mortem examination. Heart enlarged; weight 80 grammes. Right side distended with dark clotted blood. Right auricular appendage distended, and filled with roughened, corrugated, yellowish-white, parietal thrombi, which varied in size from a pin's head up to a bean. They were present also in other cavities. Joints rachitic. In addition to the above there was a chronic passive congestion and a chronic pleurisy.

No. 534. — Boy, aged six years. Had measles and pertussis. Admitted August 14. Ill for one day with nasal and faucal diphtheria. He was quite septic and continued so, and in two days had many ecchymoses on skin. Throat cleared up slowly, and he gradually lost weight. Pulse varied between 130 and 80. On the eleventh day in hospital, heart dulness from 1 cm. to right of sternum, to 2.5 cm. to left of nipple line. There was a soft systolic murmur at the apex. Sounds weak and irregular. He vomited several times. Patella and superficial reflexes all diminished. Almost complete paralysis of the palate. On the following day heart dulness had increased 1.5 cm. to right and left; pulmonic second accentuated. Pulse could just be felt, and he died on the next day, the sixteenth day of the disease.

Post-mortem examination. Heart slightly enlarged; weight 90 grammes. Muscle pale, with minute whitish specks distinctly seen on endocardium. Valves normal. There was also a diphtheritic rhinitis, tonsillitis, pharyngitis, and an acute general lymphatic hyperplasia.

Pneumogastric nerve showed an extensive degenerative process. There was hardly a single normal nerve fibre. There was much fat throughout the specimen.

Heart muscle. There was an intense and extensive degeneration of the fibres, with much swelling. The fibres had lost their striation, and were homogeneous or granular.

Throughout the interstitial tissue and near the blood vessels, and in the myocardium itself, were seen areas of infiltration of lymphoid cells.

No. 561. — Girl, aged five and one-half years. Had measles and pertussis. Admitted August 14, after two days illness, with septic diphtheria of nose and throat. There were numerous ecchymoses on skin. She was delirious throughout. Urine contained a large trace of albumin. Pulse for four days was about 125, afterwards at 70. Heart-sound weak, but regular, until the last two days, when it was irregular. Area was normal until forty-eight hours before death, then the dulness extended from 1 cm., to the right of sternum, to 2 cm. outside of nipple line. On the last day the area of dulness had increased 2 cm. more on the right and 1.5 cm. on the left. No murmur was heard. Vomited considerably during the last two days. Patella and plantar reflexes absent. Died on the ninth day of illness. No post-mortem examination.

No. 570. — Boy, seven years old. Admitted August 21 with a moderately severe attack of diphtheria of nose and throat of three days' continuance. The throat was clear within nine days. He was rather listless from the first. Heart was normal for ten days and on the thirteenth day the area of dulness extended from 1.5 cm. to the right of sternum to 3 cm. to the left of nipple line. Pulmonic second accentuated. Bruit de galop heard at apex. The next day the area of dulness had extended 2 cm. on both sides. A blowing systolic murmur at apex heard, transmitted into axilla. On the sixteenth day the area of dulness had decreased, and by the eighteenth day was from right sternal border to 3 cm. outside of nipple line. The bruit de galop was not heard on this day. The pulse varied from 80 to 120, at times irregular and intermittent. The second sound at the apex was re-duplicated. Later the irregularity and re-duplication disappeared. For a while the child seemed to be holding his own although he had lost considerable flesh. He had some paralysis of the palatal muscles. On the thirty-fifth day of illness, developed a pneumonia, after this he became again worse, vomited everything taken by mouth ; pulse very weak. Died on the forty-fourth day. No post-mortem examination.

No. 723. — Boy, aged six years. Admitted February 3, having been sick five days with diphtheria of nose and throat. For the first week did as well as the average case of diphtheria, save that he appeared drowsy all the time. Began to vomit on the twelfth day. Pulse varied from 110 to 130 and fell to 90 on the twelfth day. The following day heart dulness extended from right sternal border to 3 cm. left of nipple line. A loud systolic murmur at apex. Died in a collapse on the fifteenth day. No note as to paralysis.

Post-mortem examination. Heart much dilated; weight, 95 grammes. It extended from 4 cm. to the left of nipple line to 1 cm. beyond the rights ternal border and upward to second rib. Left side hypertrophied. On the free edge of the aortic valve were a few vegetations. Besides the above there was an acute splenitis and a hyperplasia of the mesenteric glands.

No. 728. — Boy, aged four years. Had measles and pertussis. Admitted February 3, with nasal and pharyngeal diphtheria after an illness of two days. The child was in a drowsy and stupid condition most of the time. He began to vomit on the sixth day, and continued to do so to the end. Pulse varied between 150 and 100, of weak volume and irregular in time. He gradually failed and died on the tenth day of illness. No record as to paralysis. No post-mortem examination.

Sex. — In these twenty-two cases of death from various kinds of heart failure, fifteen were males and seven were females. The fatality among the males in these cases was higher than among the 800 diphtheria cases where there were seventy-three males and forty-eight females that died.

Age. This was as follows:

Up to 2 years	3 cases.
From 3 to 4 years . . .	5 "
" 4 to 6 " . . .	10 "
" 7 to 8 " . . .	2 "
" 9 to 14 " . . .	2 "

The age varied from one and one-half to fourteen years, the average was 5.2 years.

Location of membrane.—In all but three cases it was in both nose and throat, these exceptions were one each, on tonsils, on tonsils and larynx, and on larynx. In all but four cases a more or less septic odor was noticed, and in two cases there were ecchymoses on the skin. So marked were the usual signs of sepsis in some cases that it was difficult to determine whether the cause of death was sepsis or heart failure, but after all this distinction is superficial, for most likely every case of death from heart trouble is due primarily to a toxic poisoning of the diphtheria bacillus.

Albumin.—In the fifteen cases, where the urine was examined there were eleven cases which had one-tenth of 1 per cent. or more of albumin.

The time when the first symptoms appeared, pointing to the heart, was in twenty-one cases as follows:

During the first week	. . . . .	13 cases.
" second "	. . . . .	5 "
" third "	. . . . .	2 "
" fourth "	. . . . .	1 "

The first symptom that called attention to the heart was usually a weak and irregular pulse or a very slow one. It would seem from this, that if at the end of the fourth week a diphtheria patient has had no bradycardia, feeble or arrhythmic pulse there is little possibility of death from cardiac trouble.

The number of days that the patient lived after the appearance of the first symptom varied from less than a day to five weeks, however, all but six died within less than a week.

The lapse of time from the onset of the diphtheria to when death occurred in these cases was:

Within one week	. . . .	1 case.
" two weeks	. . .	8 "
" three "	. . . .	7 "
" four "	. . . .	2 "
" five "	. . . .	1 "
" six "	. . . .	1 "
" seven "	. . . .	1 "

The average length of life was about three weeks.

A systolic murmur was noted in eight cases and all of these occurred in those which had considerable dilatation. Still, the reverse was not always true (No. 561).

The triple sound — cantering rhythm — (bruit de galop) was observed in three cases (Nos. 59, 331 and 570). It was also heard in three other cases, not included in this series two of which were fatal and one is yet in hospital and doing, well. The heart was considerably dilated in each of these patients, and the bruit de galop was noted in four of the cases when the dilatation was first determined. In both instances (Nos. 59 and 331) where the pneumogastric nerve was examined there were degenerated changes which were moderate in one and marked in the other. In these cases this cantering rhythm was then a most fatal sign.

Collapse occurred eight times, and death followed within two days in every case, and in three instances within an hour or so.

Vomiting was present in twelve of the cases. In other words, this symptom was noted in over half of these patients that died of heart trouble. Since both the heart and stomach are innervated by the same nerve, the pneumogastric, it is readily seen how a degeneration of this nerve, causing cardiac disturbances, would in a like manner produce changes in the function of the stomach, such as emesis.

The frequency of palatal paralysis in this connection is of great interest, since the innervation of the levator palati and azygos uvulae is now thought to be by the vagus, through fibres from the nucleus ambiguus.[1] If this innervation is correct, which the later writers affirm,[2] it gives an anatomical reason why all patients with palatal palsy should be kept in bed, whether or not the pulse and heart have showed any untoward symptoms, on account of the danger of a possible sudden appearance of cardiac failure.

A study was made of the weight of the hearts of these cases where there was a post-mortem examination. The table below shows the case number, the age, the duration of

[1] Kraus (in the recently published part of Nothnagel Specielle Pathologie und Therapie, Vol. xvi., p. 106) gives the above nerve supply of the palate.

[2] For the literature on this subject see Dr. J. J. Thomas' paper on "The Innervation of the Soft Palate," in the Medical and Surgical Report of the Boston City Hospital, 1896, Seventh Series, p. 171.

the illness in days, the weight in grammes of each, the average weight for the corresponding year, according to the tables in the recent text-books of Roach and Holt, and the increase in weight from those averages:

No.	Age.	Duration.	Wts.	Ave.	Increase.
59	5	17	120	72	48
63	3	29	120	65	55
105	5	15	140	70	70
325	6	43	115	75	40
331	8	21	155	100	55
363	6	10	105	75	30
369	5	21	115	72	43
400	2	9	75	55	20
463	3	8	80	65	15
534	6	11	90	75	15
723	6	15	95	75	20

In every case there was an increase of 15 grammes or more. In seven it was 30 grammes or more. The average increase was 37 grammes. As a rule this increase in weight was greater the longer the duration of the disease.

Similar tables were constructed for the cases that died of sepsis and pulmonary complications, as extension of membrane into bronchi and broncho-pneumonia. Here the increase, eliminating adults as some of them had chronic heart disease, was eleven grammes. In other words, the hearts of these diphtheria cases that died of cardiac complications showed a greater weight than those that died of pulmonary complications. Whether this increase in weight is due to œdema, the infiltration of new cells in the heart muscle, or possibly to the formation of new fibres, must be settled by the microscopic findings.

Cardiac thrombi were noted in four cases out of seventy-two that came to post-mortem examination. In three cases (369, 400 and 463) the thrombi played, apparently, an important part in the fatal result. Death was sudden in no case, but came on slowly, in one to three days. In these cases the pulse was weak in all, becoming imperceptible some hours before death. In one case (463) the rate was as low

as 54 the day before death. In another (400) it was 200. Three of the four had a systolic murmur at the apex. The patients were all cyanotic, and had cold extremeties, covered with more or less cold perspiration. The location of the thrombi were three times in the auricular appendages and twice in the left ventricle. The formation of these thrombi is explained most probably by the normally slow circulation in the auricular appendages which, in these cases, is more sluggish on account of the weak cardiac action. Another possible explanation is that the areas of degeneration that are found in the endocardium become foci for the formation of thrombi.

No. 79 is of particular interest, as it gives a reason for some of the sudden deaths that occur in intubation cases which are, naturally enough, supposed to be due to some error in the technique of the operation of intubation or extubation. In this case there can be little doubt that the degenerative changes in the nerve was primarily the cause of death, and the sudden coughing up of the tube called upon the heart for an extra and an impossible task. It is on account of this condition of the heart, why extreme care has to be used in performing any operation upon a child that has been sick for some time with diphtheria, since it requires only the slightest shock or struggle on the part of the patient to so affect the heart that death is the result.

Degenerative changes in the pneumogastric nerve of more or less severity was observed in every cardiac case where a microscopical examination was made. And, in the three cases where sections were made of the medulla some degeneration of the fibres was noted, although no changes in the nerve cells could be demonstrated by the method of staining used. It is to be regretted that the condition of the myocardium is not known in all cases. In the one examined extreme changes were observed.

The cause of these various heart complications in diphtheria, it would seem, is most probably due to the toxic action of the ptomaines or the toxalbumins generated by the Klebs-Loeffler bacillus. These poisonous substances act on the central and peripherial nervous system, producing functional and degenerative changes in the nuclei and the

nerve fibres that innervate the heart. These same toxic agents affect also the myocardium, causing various changes, while the nerve supply may, in some instances, be uninjured.[1]

Conclusions.

1. A rapid pulse-rate in diphtheria is to be dreaded. Death usually results when it exceeds 150.

2. A slow pulse — sixty in young children — is a sign often of serious heart trouble.

3. Irregularities in the pulse occur in about ten per cent. of the diphtheria cases, and are generally significant of cardiac complications.

4. A systolic murmur at the apex is heard in about one case in ten, and its prognostic value depends upon the nature of the cause.

5. A bruit de galop in diphtheria is a most fatal sign.

6. After four weeks, with no heart symptoms in diphtheria, there is little probability of subsequent cardiac trouble in the convalescence.

7. All diphtheria patients who have tachycardia, bradycardia, irregular or weak pulse, a systolic murmur at the apex, vomiting or any paralysis — especially palatal — should be kept quiet in bed.

8. The most important element in the treatment consists in absolute rest in bed.

9. The vagus nerve in the fatal cases always had some evidence of degenerative changes. The weight of the heart was increased.

10. The cause of death is usually from cardiac thrombi, dilatation or paralysis, produced most probably by the toxin of the diphtheria bacillus.

I wish here to thank those who have aided me in this paper, and especially my teacher, the resident physician, Dr. John H. McCollom, who has so kindly instructed me concerning diphtheria during the past year.

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[1] For a recent review of the literature of the histology of toxalbumin intoxication see Dr. Simon Flexner's paper on "The Pathology of Toxalbumin Intoxication," Johns Hopkins Hospital Reports, vol. vi., p. 259. 1897.

III.

ACUTE DEGENERATIONS OF THE NERVOUS SYSTEM IN DIPHTHERIA.

By John Jenks Thomas, A.M., M.D.

The changes of the nervous system produced by acute infectious diseases are various, especially those produced by diphtheria. Various writers, since Charcot and Vulpian, in 1862, have described the changes in the peripheral nerves. These are usually of the parenchymatous type, consisting of a degenerative process, due to the presence of toxic products arising, in the course of the disease, directly or indirectly from the micro-organisms producing the disease. Nevertheless, the peripheral nerves undoubtedly show at times that an interstitial process has been added to the degenerative one. As regards the central nervous system Klebs, Dejerine, Oertel, Buhl, P. Meyer, Krauss, Arnheim and Mendel all mention smaller or larger hemorrhages into the brain and spinal cord, and some of them describe processes which they considered to be a myelitis. Probably it is due to the effects of some such process as this, or to an inflammatory infiltration in the central nervous system that we see such diseases as multiple sclerosis following diphtheria, as the cases reported by Schönfeldt. More rarely we see vascular lesions of the brain, embolism, thrombosis or hemorrhage resulting in hemiplegia, as the cases reported by Henoch, Mendel, Jäckle, Auerbach, Edgren, Seifert, Donath, Apolant, Sharples, Sinkler, the writer and others. Meningitis has been described by Pierret, and Dejerine and Barth. Whether this is from an infection of the meninges by the Klebs-Loeffler bacillus, or due to infection with some of the other varieties of bacteria, so often found in the organs in cases dying of diphtheria, as by Wright, Frosch and others, will have to be determined by further investigations.

Thus we see that the changes produced in the nervous system by diphtheria are quite varied. The cases reported in this paper do not cover all the changes of the nervous structures in this disease, but show somewhat the extent of the acute degenerative changes produced by it. It is hoped that in a future paper some other points in the changes of the nervous system in diphtheria can be taken up, particularly the changes in the nerve cells as shown by Nissl's stain. These investigations were begun with the intention of seeing whether or not degenerative changes were common in the pneumogastric nerves of cases dying suddenly from failure of the heart during diphtheria, or during convalescence. Later, examinations were made of other nerves of the central nervous system, and of the heart muscle. While the number of cases is small it seems to be enough to warrant us in drawing a few general conclusions. For the clinical notes of these cases I have to thank Dr. C. M. Hibbard, of the South Department, and the reports of the autopsies and results of cultures have been abstracted from the records of the pathological department of the Boston City Hospital with the kind permission of Dr. W. T. Councilman.

The cases are as follows: The numbers in parenthesis refer to the numbers in the articles by Dr. J. H. McCollom and Dr. C. M. Hibbard.

Case I. — Boy, about ten years. Had been ill three days on entrance. Voice weak. On fifteenth day vomited; shortly after became pale and restless, with rapid and very feeble pulse. After some hours became more quiet, but respiration was rapid and he was still pale, almost cyanotic. Respirations rose to 70. Pulse feeble, and died about five hours after onset of symptoms. The membrane at this time had disappeared. Diphtheria bacilli were found on the eleventh day, however. There was no note of paralysis.

Autopsy. — Sept. 13, 1895. Boy, about ten years. Body length, 127 cm. *Heart*, enlarged and cavities dilated, especially the right auricle, which was filled with dark clotted blood. Weight, 180 grammes. On opening the left ventricle several round, organized, pea-sized or smaller thrombi were found surrounding the chordæ tendineæ. The cusps of the aortic valve were thickened and somewhat retracted, and

along their line of closure there were a number of pin-point sized grayish vegetations. No membrane in *pharynx* or *tonsils. Anatomical diagnosis;* endocarditis, chronic fibrinous endocarditis of aortic valve, insufficiency of aortic valve, general dilatation and hypertrophy of heart, chronic passive congestion of liver, kidneys and spleen, anæmia and cloudy swelling of liver, acute splenic tumor, chronic passive congestion of lungs, acute mesenteric lymphatic hyperplasia. No cultures.

Microscopical examination; Pneumogastric nerve. Sections showed a most intense and extensive degeneration of nerve fibres. It was impossible to find a fibre which was not affected in most of its course. The amount of fat in the nerve sheaths and axis cylinders was large. Many nerve fibres were represented by a chain of larger and smaller fat drops, with here and there a grayish outline of the fibre visible. In places the axis cylinder could be made out, but when present it was swollen and beaded or broken, and in many fibres no axis cylinders could be made out, but only the beaded, irregular fibre, containing many fat drops, could be seen.

Case II. — Girl, age two years. Was admitted with septic diphtheria. Pulse regular, rapid and strong. On the second day vomited. There was a discharge from the ears which ceased three days before death. On seventeenth day, had a convulsion in the evening, and an hour and a half later clonic spasms, which continued for half an hour when death ensued. The examination of the urine was negative.

Autopsy. — Sept. 4, 1896. Clinical diagnosis, diphtheria. Slight congestion of the *trachea. Heart:* weight, 50 grammes (normal). *Brain:* normal. *Anatomical Diagnosis*: chronic pericarditis, general lymphatic hyperplasia, sub-acute splenitis. *Cultures:* Heart, sterile. Liver, staphylococcus pyogenes aureus. Spleen and kidneys, sterile.

Microscopical examination: Pneumogastric nerve. — Many fibres were seen which were grayish in color, granular and swollen, with swollen and beaded axis cylinder. In a few of these fibres there were fat drops. About half of the fibres seemed affected. Sections of the *obturator nerve* showed the

same changes to be present in this nerve, but to a more marked degree. Almost all the fibres were affected, and fat globules were present in large numbers. *Anterior crural nerve:* Here there were similar changes affecting a large majority of the fibres, but fat, while present, was not seen in such amounts as in the obturator nerve. *Lumbo-sacral cord.* These sections showed an extensive degeneration. Most of the nerve fibres were affected to a greater or less extent. The amount of fat showed considerable variation. In places it was present in moderate amount, while in other places almost every nerve fibre showed the presence of numerous fat globules.

Case III. — Boy, age six years. Admitted with diphtheria. At first there was albumin in the urine, which later diminished to a mere trace. On twelfth day, vomited. Pulse became weaker and more rapid, and the child died on the thirteenth day in collapse. There was no note of paralysis.

Autopsy. — Sept. 11, 1896. *Heart:* weight 135 grammes. Left ventricle dilated. Mitral valve insufficient. Foramen ovale patent. *Brain* was normal except for increase of fluid in the ventricles. *Anatomical diagnosis:* Open foramen ovale, general ascites, follicular enteritis. Trachea, larynx, etc., normal. No cultures.

Microscopical examination; Pneumogastric nerve. — Cross section. Few fibres showed replacement of axis cylinder or myelin sheath by fat. Almost all showed a brownish discoloration, and in many myelin sheaths the grayish ring was irregular and of varying thickness. Some fibres were much swollen. The axis cylinders had lost their refractive appearance, and sometimes had entirely disappeared. Longitudinal sections. There were a few fat globules in the nerve sheaths and inside them. The sheaths were stained grayish, and were very irregular, striated and granular in appearance. The axis cylinder, when present, was grayish in color and much beaded. Many of them were broken into short masses, some normal in color, others stained gray. In many cases the axis cylinder could not be made out. *Phrenic nerve:* changes similar to those seen in the pneumogastric nerve were found, but less marked, and only about half the fibres seemed affected. *Splanchnic nerve:* seemed perfectly normal.

Semi-lunar ganglion: showed no marked fatty changes of fibres or cells. *Heart:* the muscular fibres of the heart had lost in part their striations, though in most of them longitudinal striations could be seen. Some of the fibres had a homogeneous appearance. Very rarely fibres were seen containing fat drops, and occasionally one containing a vacuole. Many of the small blood vessels were dilated, and filled with blood, and there were occasional hemorrhages into the connective tissue about the blood vessels. Here and there throughout the connective tissue, sometimes in the neighborhood of a blood vessel, there were infiltrations of small, round lymphoid cells, with round, deeply staining nuclei and little protoplasm. There were also occasional larger cells, with less deeply staining, granular nuclei and more protoplasm. Similar areas of infiltration were seen here and there in the muscular substance.

Case IV. — Woman, age sixty-one years. Admitted with septic laryngeal and faucial diphtheria, broncho-pneumonia, asthma and cardiac disease. She had been ill two days. She had vomiting. Cultures from the throat showed pure diphtheria baccillus growth. The clinical diagnosis of diphtheria in all cases was made only after examination of cultures from the throat. She had some difficulty in breathing (asthma). Pulse regular. On the third day after admission she had a sudden collapse. Respiration very rapid. Very cyanotic. Pulse very weak. She had had a nasal voice, and regurgitation of fluids through the nose.

Autopsy. — Feb. 22, 1897. Clinical diagnosis, diphtheria. *Tonsils* enlarged and reddened; in places covered by small patches of grayish white, rough pseudo-membrane, which could be easily removed, leaving a red surface. Beginning near the tip of the *epiglottis*, a thick, dirty gray membrane extended through the *larynx* and *trachea* into the bronchi. This membrane could be easily removed, leaving a rough, red, angry surface. The membrane could be followed in the bronchi of the lung beyond the fourth bifurcation, as far as the bronchi could be recognized and laid open. On section of the lung there were seen in the small bronchi small white dots of membrane, which could be removed with forceps, bringing with them membrane, extending into the

bronchioles, and forming a perfect cast of the air vessels. *Heart:* weight, 330 grammes. Much pericardial fat. Heart muscle flabby, of brownish red color. On the surface of the papillary muscle, here and there, were yellowish spots in marked contrast with the darker heart muscle. In frozen sections the heart muscle was seen to contain small accumulations of fat in extremely small droplets. The valves and cavities otherwise normal. Coronary arteries dilated, tortuous, with walls irregularly thickened in places, and calcarious. *Anatomical diagnosis.* — Diphtheritic tonsillitis, laryngitis, tracheitis, and bronchitis, œdema of lungs, fatty myocarditis, arterio-sclerosis, acute splenic tumor, acute parenchymatous degeneration of liver and kidneys, fibroids of uterus, chronic peritonitis. *Cultures:* Right lung, lower lobe abundant Klebs-Lœffler bacillus. Liver and kidney, colon bacillus. In lung, liver, spleen and kidneys there was also an organism which grew in raised bead like colonies, which stained faintly with Lœffler's methyl-blue stain, but well with fuchsin and carbol-gentian violet stains. It was oval, or rather elongated, in form, with a suspicion of a capsule. Reddened litmus milk. Not motile.

Microscopical examination; Pneumogastric nerve: Sections stained by Marchi's method showed marked degeneration, scarcely any of the fibres being free from changes. These varied considerably in degree, from grayish discoloration and granular appearance of the nerve sheath and axis cylinder to disappearance of the latter and replacement of it, and of the myelin sheath to greater or less extent by fat drops. The fibres least affected appeared granular and beaded, and the axis cylinder even in these fibres could not always be distinguished.

Case V. — Girl, about two and one-half years, was admitted with septic laryngeal diphtheria, and had had seven hemorrhages. She had been ill for six days. The pulse was very weak. The child was intubed at once, but did not breathe any better, so the tube was removed, and she died almost immediately.

Autopsy. — March 2, 1897. Clinical diagnosis, diphtheria with hemorrhage. *Heart:* weight, 75 grammes. Valves and cavities normal. *Trachea* and *bronchi* down to the

third division of the bronchi showed a firm, well formed membrane which was stained with blood. The bronchi were filled with blood. The membrane was very well marked in the larynx area around the epiglottis, where it had become slightly separated. The membrane extended up over the pharynx and tonsils, and slightly inwards over the tongue. The origin of the hemorrhage could not be found. *Anatomical diagnosis:* acute diphtheritic tonsillitis, laryngitis, epiglottiditis, tracheitis and bronchitis with hemorrhage, acute broncho-pneumonia of right lung, with hemorrhage, acute swelling of liver and kidneys, acute lymphatic hyperplasia, acute splenitis. *Cultures*, trachea, many Klebs-Loeffler baccilli; lung, liver and spleen, streptococci and Klebs-Loeffler baccilli; kidney many Klebs-Loeffler bacilli.

Microscopical examination; Pneumogastric nerve: The sections showed a considerable amount of degeneration, and the presence of a moderate amount of fat in the nerve fibres. Many of the myelin sheaths were granular, irregularly swollen and broken. The axis cylinders were much beaded and broken. Fully one-half of the nerve fibres showed changes, more or less marked.

Case VI. (3) — Boy, age two years. Admitted with laryngeal diphtheria, and lived two days. Died of broncho-pneumonia. No heart symptoms. Pulse varied between 145 and 175. No paralysis noted.

Autopsy. — March 15, 1897. Clinical diagnosis, diphtheria. *Heart:* weight, 80 grammes. Valves and cavities normal. Pericardium normal, except that it contained about 20 cc. of clear fluid. *Trachea* as far down as the bifurcation, and the *larynx* showed a firm, grayish membrane, which in some places was separated from the trachea, and showed beneath a newly-formed membrane. The *epiglottis*, on its under surface, was covered with membrane. The *pharynx* showed small spots of this same membrane, and the *tonsils* showed excavations which were lined with this same membrane. *Anatomical diagnosis:* acute diphtheritic tonsillitis, pharyngitis, epiglottiditis, bronchitis and laryngitis, acute broncho-pneumonia of upper and lower lobes of right lung, general acute lymphatic hyperplasia. *Cultures:* right lung, upper and lower lobes, streptococcus; liver, streptococcus (pure);

spleen, streptococcus; kidney, an organism resembling the pneumococcus, occurring in short chains, but not the streptococcus; right middle ear, few streptococci.

Microscopical examination; Pneumogastric nerve. Sections from this case show a considerable number of fibres affected. They were swollen and granular in appearance, and in the greater part of them fat globules could be seen in some part of their course. The axis cylinders in the fibres most affected were absent, and in others were swollen and beaded.

Case VII. (63) — Boy, age three years. Was admitted March 3, 1897, with diphtheria, and went home in eight days. Thirteen days later was readmitted with some symptoms of laryngitis. Nine days later, or on the thirtieth day from the first admission, the pulse, which had varied between 110 and 130, became more rapid and so weak it could not be counted, and the child died in collapse. He had had a nasal voice.

Autopsy. — April 3, 1897. Clinical diagnosis, diphtheria. *Tonsils* and *pharynx* normal, except that the tonsils were very much enlarged, and granular. The larynx was normal, the epiglottis was covered with a whitish membrane, which was quite firm, and required some force to remove it. This membrane covered only the epiglottis, and did not extend through any part of the larynx. The mucous membrane of the larynx was hyperemic, otherwise normal. *Heart:* weight, 120 grammes. Valves and cavities normal. *Brain:* weight, 1,390 grammes, normal. *Anatomical diagnosis:* diphtheritic epiglottiditis, acute broncho-pneumonia of upper lobe of left lung, hydrothorax, hydro-pericardium, general acute lymphatic hyperplasia. *Cultures:* lung, streptococci; liver, abundant streptococci, one colony of Klebs-Loeffler baccillus; spleen, negative; kidney, sterile.

Microscopical examination; Pneumogastric nerve. Sections showed the presence of a considerable number of fibres which were stained gray, and of which the myelin sheath was irregular, swollen, granular and broken. The axis cylinders could usually be distinguished, but they were swollen, beaded and broken. Fat drops were few in number. The greater part of the fibres showed no changes.

Case VIII. (78). — Boy, age nine months. Admitted with diphtheria of the nose, cultures being positive, after an illness of seven days. Lived six days. No paralysis noted.

Autopsy. — April 7, 1897. Clinical diagnosis, post-diphtheritic cardiac paralysis. *Brain:* weight, 880 grammes. Vessels of pia injected, otherwise brain was normal. *Tonsils*, *pharynx* and *larynx* normal. On the under surface of the *epiglottis*, near the base, on the right side, there was a small patch of grayish-yellow membrane, beneath which the mucous membrane was rough and red. On the other side the mucous membrane was rough and of a dull red color. *Trachea* normal. *Heart:* weight, 50 grammes. Valves and cavities normal. *Anatomical diagnosis:* diphtheritic epiglottiditis, constriction of œsophagus, broncho-pneumonia and bronchitis, general lymphatic hyperplasia. *Cultures:* Right lung, upper lobe, streptococcus, and abundant Klebs-Loeffler bacillus; liver, Klebs-Loeffler bacillus and streptococcus; spleen, streptococcus (pure); kidneys, streptococcus; right middle ear, abundant streptococcus, few Klebs-Loeffler bacilli, and two colonies of styphylococcus pyogenes aureus.

Microscopical examination: Pneumogastric nerve. Sections showed marked degenerative changes. Most of the fibres contained fat drops, some of them in large numbers. The nerve sheaths did not show any marked granular changes, but were much swollen and broken. The axis cylinders were absent in many cases, being replaced by drops of fat. In other fibres they appeared beaded, or were fairly normal.

Case IX. (79). — Boy, aged three years. Admitted after an illness of five days, and lived ten days after admission. The child had laryngeal diphtheria, and was intubed. He coughed the tube up, and died suddenly. No paralysis noted.

Autopsy. — April 11, 1897. Child, of apparently one and one-half years. *Tonsils*, *pharynx*, *larynx* and *trachea* normal. *Heart:* weight, 65 grammes. Valves and cavities normal. Pericardium normal. *Brain:* slight edema of pia, otherwise normal. *Anatomical diagnosis:* acute general lymphatic hyperplasia, acute splenitis, toxemia (?). *Cultures:*

heart blood, streptococcus; liver, streptococcus; spleen, streptococcus; kidney, few stroptococci.

Microscopical examination; Pneumogastric nerve. Sections showed marked degenerative changes of most of the nerve fibres. The nerve sheaths were grayish in color, granular and swollen, and showed the presence of considerable fat. The axis cylinder was often absent, and when present was usually beaded or broken, and replaced by fat drops.

Case X. (331). — Boy, age eight years. Had been ill for ten days when admitted. For ten days the pulse varied between 70 and 100. On the tenth day the pulse rose to 134 and became weak. He vomited. Extremities were cold. There had been a marked nasal tone to the voice, and the knee-jerks were diminished. On the thirteenth day of his stay in the hospital, and the twenty-first day of the disease the face became pale, the lips cyanotic, while the pulse rose to 200, and became intermittent, and the child died.

Autopsy. — June 13, 1897. Clinical diagnosis, diphtheria. *Heart:* left ventricle greatly dilated; mitral valve admitted tips of three fingers; weight, 155 grammes. *Pharynx*, *trachea*, etc., normal. *Brain*: weight, 1,250 grammes. Much fluid beneath the pia. Brain substance rather moist. *Spinal cord*, normal. *Anatomical diagnosis:* dilatation of heart. *Cultures:* sterile.

Microscopical examination; Pneumogastric nerve. Sections showed a diffuse degeneration of nerve fibres of moderate intensity. The myelin sheaths were stained gray in color, and were much swollen, while many were broken, but few showed any granular appearance. In many instances the axis cylinder could not be made out, but in others it was swollen and beaded. Fat globules were rare. The *sciatic nerve* showed about as extensive degeneration as the pneumogastric, but fat was present in moderate amounts. The *anterior crural nerve* showed similar changes, but affecting almost all the nerve fibres, and more intense, while fat was present in the nerve structures in large quantities. *Spinal cord:* the membranes of the cord were normal. The *nerve roots*, both anterior and posterior, showed extensive degeneration; Many of the nerve fibres showed the presence of fat drops in, or replacing the myelin sheath. In many of these degener-

ated fibres the axis cylinder had disappeared, sometimes being replaced by a fat drop, while at other times no sign of it could be seen. In the *white substance* of the cord there was a moderate diffuse degeneration of nerve fibres. In many cases the axis cylinder was replaced by a drop of fat. In others the myelin sheath was represented by a complete or broken ring of fat with empty centre, or containing a swollen axis cylinder. Again, the nerve fibre was represented by a large drop of fat replacing both sheath and axis cylinder. This degeneration was found in all parts of the white matter, but was somewhat more extensive in the posterior columns. In the *gray matter* of the cord the blood vessels appeared dilated, but no hemorrhages were found there or in any other part of the cord. Occasional degenerated fibres showing fat drops were seen throughout the gray matter. The nerve cells of the *anterior horn* showed practically no changes; there was no fat present in them. In a few cases the nucleolus stained poorly and was irregular in outline. Occasionally a cell was seen which appeared shrunken. In a few cases the processes were separated from the cell body—probably an artefact. The nerve cells of other parts of the gray matter appeared normal. The *neuroglia* did not appear increased. Sections of the *medulla* at the upper part of the pyramidal crossing showed the same diffuse degeneration of the nerve fibres. The nerve cells appeared normal. Sections of the *pons* showed a marked degeneration of the fibres of the superior cerebellar peduncle with the presence of much fat. The fibres of the formatio reticularis showed a slight diffuse degeneration with a small amount of fat. There was a marked degenerative process in the root of the fifth nerve with a large amount of fat. Sections of the cortex of the *brain* were practically normal, although occasionally a fibre was seen which showed the presence of fat.

Case XI. — (363). Boy, age six and one-half years. This was a septic case, with a total duration of ten days. There was vomiting. Albumin was present in the urine. The heart's action was regular. Pulse weak. He had regurgitation of fluids through the nose.

Autopsy. — June 21, 1897. Clinical diagnosis; diphtheria. There was a grayish membrane on the *tonsils*, and

the upper part of the *oesophagus*. *Heart:* weight, 105 grammes. Muscle red and moist. Left ventricle slightly dilated. Mitral valve admits two fingers beyond the first joint. Wall from 0.5 to 1.2 cm. thick. The other valves and cavities were normal. *Brain:* weight, 1,340 grammes. Soft in consistency, but otherwise normal. *Anatomical diagnosis:* diphtheritic tonsillitis and oesophagitis, chronic fibrinous pleuritis, slight emphysema of lungs, acute congestion of liver, tuberculosis of cervical and mesenteric lymph glands, acute general lymphatic hyperplasia. *Cultures:* heart, spleen and brain sterile; liver, Klebs-Loeffler bacillus (pure); kidney, Klebs-Loeffler bacillus, colon bacillus and staphylococcus albus; right middle ear, Klebs-Loeffler bacillus, and staphylococcus pyogenes aureus; left middle ear, staphylococcus pyogenes aureus, and a very few Klebs-Loeffler bacilli.

Microscopical examination; Pneumogastric nerve. Sections showed a moderately extensive degeneration. A majority of the nerve fibres had swollen and broken myelin sheaths with a considerable amount of fat present. The axis cylinders had often disappeared and in other cases were irregular and beaded in outline, and broken by fat drops.

Case XII. — (400). Girl, age two and one-half years. On admission had been ill three days. She had nasal and faucial diphtheria, with some prostration. Pulse 100-120. The pulse failed gradually, the lips became cyanotic, and the extremities cold. There was no note of paralysis. The child died on the eighth day of the disease.

Autopsy. — June 27, 1897. Clinical diagnosis, diphtheria. *Heart:* weight, 75 grammes. In the left ventricle there was a firm thrombus, attached to the interventricular septum. The valves were normal. The *tonsils* were deeply ulcerated. There was pus in the right *ear*. *Brain:* weight, 1.195 grammes. It was moderately injected. *Anatomical diagnosis:* ulceration of tonsils, diphtheritic rhinitis, otitis media. *Cultures:* heart, streptococcus; liver, spleen and kidney, sterile; right ear, staphylococcus aureus and a few Klebs-Loeffler bacilli.

Microscopical examination; Medulla. — Sections at the level of the pyramidal crossing showed a moderate amount of degeneration, with the presence of considerable fat in the

pyramidal fibres. The degenerative process had also affected the fibres of the posterior tracts, but to a rather less extent. The nerve cells were normal. Sections from the cortex of the *brain* showed the presence of an occasional fat drop in a few fibres. Sections of the *pneumogastric nerve* showed a slight but rather extensive degeneration. A considerable number of fibres showed swollen and granular myelin sheaths, stained grayish in color, and the presence of a small amount of fat. The axis cylinders were many of them swollen and beaded.

Case XIII. — (325). Boy, age six years. The pulse in this case varied between 70 and 120. There was albumin in the urine. Paralysis of the palate was noted on the forty-first day of the disease. The child died on that day with heart symptoms.

Autopsy. — July 9, 1897. Clinical diagnosis, diphtheria, *Heart:* weight, 115 grammes. Normal. *Brain:* 1,240 grammes. Normal. There was pus in the right *ear*. *Anatomical diagnosis:* edema of lungs, otitis media. *Cultures:* heart, negative; spleen, sterile; kidney, colon bacillus and staphylococcus albus; liver, colon bacillus and staphylococcus citreus; lung, streptococcus and Klebs-Loeffler bacillus.

Microscopical examination; Pneumogastric nerve. — Sections showed very slight degenerative process. A few fibres were much swollen, irregular in outline, beaded, and stained grayish. The axis cylinders of these fibres were irregular and beaded. Rarely a few fat drops could be seen in the myelin sheath.

Case XIV. — (494). Woman, age, 64 years. This was a septic case, which was delirious. The total duration was about three weeks. The patient died from extension of the membrane. The pulse was weak and rapid, but regular.

Autopsy. — July 16, 1897. Clinical diagnosis, diphtheria. *Heart:* weight, 210 grammes. Muscle dark brown in color. Valves normal. There was membrane on the *pharynx*, *tonsils*, epiglottis, onto the tongue, and beginning of *œsophagus*, down to the *larynx* and whole of the *trachea*, into the primary *bronchi*. *Anatomical diagnosis:* diphtheritic pharyngitis, tonsillitis, uvulitis, laryngitis, glossitis, tracheitis, and bronchitis, broncho-pneumonia, emphysema of lungs, edema of lungs, chronic passive congestion of spleen, kidneys and liver.

Cultures: heart, negative; lung, Klebs-Loeffler bacillus and pneumococcus; liver and spleen, sterile; kidney, few Klebs-Loeffler bacilli, and colon bacillus.

Microscopical examination; Pneumogastric nerve.—Sections showed a large majority of the fibres grayish in color, granular, and some intensely swollen. Fat was present in moderate amounts. The axis cylinders in the affected fibres could not usually be made out, but when present were beaded, irregular and broken.

Case XV.—(105). Boy, age five years. The child was admitted to the hospital in a septic condition, and died within twenty-four hours, after an illness of two weeks. No note of paralysis. Pulse was 79 and weak.

Autopsy.—July 20, 1897. Clinical diagnosis, diphtheria. *Heart:* weight, 140 grammes. Left ventricle dilated. No valvular lesion. *Brain:* weight, 1,450 grammes. Normal. *Anatomical diagnosis:* diphtheritic pharyngitis, laryngitis, etc., dilatation of heart, chronic passive congestion, ascites, hydrothorax. *Cultures:* heart, liver and kidneys, colon bacillus; spleen, colon bacillus and Klebs-Loeffler bacillus; lung, Klebs-Loeffler bacillus, and a few streptococci.

Microscopical examination; Pneumogastric nerve:—Sections showed rather a slight degenerative process. A moderate number of fibres were grayish in color, and irregular in outline, with occasional fat drops. The axis cylinders were swollen and beaded in the affected fibres.

Case XVI.—(59). Boy, age five years. Duration of the disease was fifteen days in all. The child was languid. Four days before death the pulse was irregular and weak (130). He vomited twice. There was a partial collapse the day before the child died. There was no note made of paralysis. The pulse the last day was weak and intermittent.

Autopsy.—July 30, 1897. Clinical diagnosis, diphtheria. Slight increase of pericardial fluid. *Heart:* weight, 120 grammes. All cavities were much dilated, and filled with post-mortem clots. No endocardial changes. Auriculo-ventricular valves, especially the mitral, were dilated. Heart muscle yellowish and opaque, probably due to fat. *Trachea, larynx*, etc., nothing abnormal to be seen. A little pultaceous

material covered the tracheal mucous membrane. Right tonsil slightly enlarged, and follicles large and open. *Brain:* weight, 1,295 grammes. Very edematous. Lateral ventricles enlarged, and filled with clear fluid. The roof of thalami showed a peculiar roughness and looseness of tissue, which might be due to strain of edematous tissue. *Anatomical diagnosis:* dilatation of heart, congestion and edema of lungs, congestion and fatty degeneration of liver, acute splenic hyperplasia, chronic passive congestion and infarction of kidneys, healed tuberculosis of mesenteric lymph glands, defects of skull through irregular union of coronal suture, with adhesion of membranes, and local atrophy of brain. *Cultures:* heart, negative; liver, colon bacillus and streptococcus; spleen, abundant streptococcus (pure); kidney, streptococcus and colon bacillus; sphenoidal sinus, streptococcus and a variety of non-pathogenic bacteria.

Microscopical examination; Pneumogastric nerve. — In this case there was marked and extensive degeneration. The sections showed a large proportion of the nerve fibres affected to a greater or less extent. Most of the fibres were swollen and grayish, and in many of these there were present considerable amounts of fat, both in the nerve sheath and in the axis cylinder. The axis cylinders were absent in most of the fibres most affected, and were irregularly swollen in the other fibres. Sections from the *floor of the fourth ventricle* showed the presence of fat in the nerve sheath, and in some instances replacing the axis cylinder, in a considerable number of the nerve fibres seen. The nerve cells seemed normal. Sections from the cortex of the *brain* showed a moderate amount of fat along the nerve fibres. The nerve cells were apparently unaffected.

Case XVII. (534). — Boy, age six years. Had been ill one day, when admitted, with faucial and nasal diphtheria. Was quite septic on admission. Throat cleared up slowly. Pulse 80-130. Forty-eight hours before death pulse became weak and irregular. Vomited on the last day. Noted that he had almost complete paralysis of the soft palate. Patellar and superficial reflexes were all diminished.

Autopsy. — Aug. 14, 1897. Clinical diagnosis, post-diphtheritic cardiac paralysis. Body of boy about six years, 112

cm. long. Pericardial cavity normal. *Heart:* weight, 90 grammes. Muscle pale, with minute whitish specks distinctly seen on endocardium. Cavities and valves normal. Left *tonsil* showed a deep loss of substance, with thin pale membrane. Right tonsil enlarged and hyperemic. *Œsophagus* and *trachea* normal. *Brain*, weight, 1,380 grammes, normal. Membranes normal. *Anatomical diagnosis:* ulceration of left tonsil, acute rhinitis, tonsillitis, pharyngitis, mucoid degeneration of sphenoidal sinuses and left middle ear, fatty degeneration of heart muscle, chronic adhesive pleurisy, general acute lymphatic hyperplasia. *Cultures:* heart and liver, sterile; spleen, colon bacillus, and pyocyaneus; kidney, colon bacillius; sphenoidal sinus, almost pure growth of a large coccus growing in straight chains; left ear, pyocyaneus, and a bacillus resembling in growth and morphology the colon bacillus, but not stained by Loeffler's methyl-blue stain.

Microscopical examination; Pneumogastric nerve. Sections showed extensive degenerative processes, hardly a single nerve fibre being free from changes. The myelin sheaths were granular and irregular, and all through the specimens there were many fat drops, chiefly small, and in the nerve sheaths. In some fibres the axis cylinder could not be made out, and in most fibres they were irregular and beaded. Sections of the *cauda equina* showed a moderate number of fibres with granular myelin sheaths, and occasionally fat drops were seen in the sheaths. The axis cylinders were occasionally beaded, but in general appeared normal. Sections of the *spinal cord* showed an extensive degeneration of the fibres of the anterior nerve roots with granular nerve sheaths and a moderate amount of fat, and a less extensive degeneration of the posterior nerve roots. There was a very extensive and intense degeneration of the posterior root zone of the cord, with a large amount of fat. Throughout the cord, there was a moderate amount of degeneration of the fibres of the *white substance*, slightly more marked in the posterior columns, involving both nerve sheaths and axis cylinders, shown by the presence of larger and smaller fat drops. This was most marked at the periphery of the cord (lack of penetration of the osmic acid). The blood vessels were

widely dilated at various places. The central canal was very much dilated, and a few red blood corpuscles were seen within it. The cells of the *gray matter*, and the fibres of this part of the cord appeared normal. Sections of the *heart muscle*, stained by Marchi's method showed a most extensive and intense fatty degeneration of the muscle fibres. Many of the fibres contained larger and smaller drops of fat, many of them being completely filled with these drops. The fibres containing fat appeared swollen, as did many of the others. Most of the fibres had lost their striations and appeared homogeneous or granular. Here and there throughout the tissue there were areas of infiltration with round lymphoid cells, which had large deeply staining nuclei and little protoplasm. These areas were found chiefly in the interstitial tissue, and about the blood vessels, but a number of them were found in the myocardium itself.

The following cases were of diphtheria accompanied by scarlet fever in which histological examinations of the nerves were made.

Case XVIII. — Girl, age seven years. Admitted on second day of the disease with diphtheria, was up on the sixth day. On the ninth day the rash of scarlet fever appeared. Membrane appeared on the tonsil. Cultures from the throat were positive. The pulse became rapid. Temperature 103°-104°. Urine of acute nephritis.

Autopsy. — Feb. 18, 1897. Clinical diagnosis, diphtheria and scarlet fever. Dull red papular eruption on thighs, upper arms, neck and trunk. *Heart:* normal size. Pericardium contained a small quantity of clear serous fluid. Valves and cavities normal. Edges of *tonsils* raw, reddened and swollen, and covered with muco-pus. *Trachea* and œsophagus normal. *Anatomical diagnosis:* scarlet fever, congestion and edema of lungs, pericardial effusion, acute splenic tumor. *Cultures*: trachea, variety of bacilli, few streptococci, no Klebs-Loeffer bacilli; lungs, many streptococci; liver, few streptococci, and about twenty-five colonies of staphylococcus aureus; spleen, many streptococci (pure); kidney, one colony of staphylococcus aureus and a few colon bacilli.

Microscopical examination; Pneumogastric nerve. Sections showed an occasional degenerated nerve fibre, with re-

placement by fat drops, and disappearance or beading of the axis cylinder, and a few granular and brownish discolored fibres, but the sections in the main were normal.

Case XIX. — Boy, age three years. Entered the hospital with measles and diphtheria. Had been ill two days. On the eighth day of the disease temperature rose, throat was red, and the tonsils swollen. A culture five days before had been negative. That evening became cyanotic. Respiration was rapid. Extremities cold. Pulse scarcely perceptible, and the child died soon after.

Autopsy. — Feb. 20, 1897. Dull red papular eruption on trunk, neck and face. *Tonsils* swollen, and mucous membrane about them raw and red. *Heart:* weight, 80 grammes. Valves and cavities normal. The *trachea* and *œsophagus* were normal. *Anatomical diagnosis:* scarlet fever, bronchitis and broncho-pneumonia, acute hyperplasia of mesenteric lymph glands. *Cultures:* liver, sterile; spleen, Klebs-Loeffler bacillus fairly abundant; kidney, a few colonies of Klebs-Loeffler bacillus; left lung, abundant growth of discrete colonies (about 100) of Klebs-Loeffler bacillus, and one colony of staphylococcus pyogenes aureus; right lung, Klebs-Loeffler bacillus and staphylococcus present, but colonies were not distinct on account of the presence of a liquefying bacillus.

Microscopical examination; Pneumogastric nerve. The sections showed marked changes. About one-half of all the fibres showed the presence of fat globules in the myelin sheath, which was much broken, irregular and swollen. The axis cylinders were swollen, beaded, broken and occasionally could not be made out. Rarely could a fibre, which appeared normal, be traced any distance without showing signs of degeneration.

Case XX. — Girl, age fourteen months, a sister of the previous case, entered the hospital after an illness of two days, with measles and diphtheria. On the fourth day of her stay in the hospital developed the eruption of scarlet fever. Three days later was only semiconscious, and died the next day, the tenth day of the disease.

Autopsy. — Feb. 21, 1897. Dull brownish papular eruption on arms and face. Right side of face swollen. *Tonsils* en-

larged and reddened. Mucous membrane of *pharynx*, *larynx* and *trachea* injected. No evidence of membrane. *Heart:* weight, 33 grammes. Valves and cavities normal. Pericardium normal. *Anatomical diagnosis:* acute fibrinous pneumonia and pleurisy of left lung, broncho-pneumonia of right lung, general lymphatic hyperplasia. *Cultures:* trachea, few Klebs-Loeffler bacilli: and streptococcus; left lung, lower lobe, staphylococcus aureus and albus and colon bacillus; left lung, upper lobe, few Klebs-Loeffler bacilli, staphylococcus aureus and albus, and colon bacillus; right lung, staphylococcus albus and streptococcus; liver, colon bacillus and bacillus fœtidus; spleen and kidney, bacillus fœtidus.

Microscopical examination; Pneumogastric nerve.— Sections showed well marked degenerative changes. Many of the fibres contained fat globules, and the sheaths were swollen and irregular. The axis cylinders of these fibres were absent or beaded.

Case XXI. — Boy, age three years. Admitted with diphtheria. On the second day the eruption of scarlet fever appeared. Pulse was rather rapid, between 90 and 160. There was albumin in the urine. The child was drowsy. On the twentieth day he had a general tonic convulsion. Another one occurred one hour later, in which he died.

Autopsy. — Feb. 27, 1897. Body, 90 cm. long. Skin desquamating over upper chest, back, and upper arms. *Heart:* weight, 55 grammes, large. Muscle, dull red, moist. Left ventricle dilated. Mitral orifice dilated. Valve incompetent. Valves otherwise normal. Pericardium distended by large accumulation of clear serous fluid. *Anatomical diagnosis:* acute interstitial nephritis, pericardial effusion, dilatation of left ventricle, edema of lungs, chronic passive congestion of lungs, liver and spleen, acute hyperplasia of abdominal lymph glands. *Cultures:* trachea, few streptococci; right lung, lower lobe, few Klebs-Loeffler bacilli, staphylococcus aureus and albus; liver and spleen sterile; kidneys, four tubes, three sterile, one showed a very few short chains of streptococci and a few Klebs-Loeffler bacilli.

Microscopical examination; Pneumogastric nerve. — The sections showed marked and extensive changes. Scarcely

any fibres could be found which did not show the presence of fat globules in some part of the distance through which they could be traced. The myelin sheaths were swollen and broken, as were also the axis cylinders, and practically all the nerve sheaths showed a granular appearance when fat drops were not present.

Case XXII.—Boy, age five years. Admitted with septic diphtheria. Had been ill two days. On the ninth day of disease it was noted that he was dull and vomited. On the twelfth day he had improved somewhat. On the twentieth day he developed the rash of scarlet fever. He had paralysis of both legs, and could not stand nor move the limbs. The knee-jerks were absent and the plantar reflex slight. On the thirty-second day he became drowsy, vomited, and died.

Autopsy. — March 2, 1897. *Heart:* large, found in diastole. Muscle moist. Slight thickening in right mitral curtain. Left ventricle dilated. Some yellow, opaque areas in middle aortic cusp, over corpora aurantia. Right ventricle showed slight degeneration. Pericardium normal. *Larynx* normal. *Tracheal* mucous membrane injected, covered by a tenacious mucus-like exudate, which was easily separated. *Oesophagus:* normal. *Anatomical diagnosis:* dilatation of left ventricle, slight arterio-sclerosis, congestion and broncho-pneumonia of lungs. *Cultures:* trachea, negative; right lung, lower lobe, six colonies of staphylococcus pyogenes aureus and a few Klebs-Loeffler bacilli, degenerated forms; liver and spleen, sterile; kidney, four colonies of staphylococcus aureus, Klebs-Loeffler bacillus, and streptococcus.

Microscopical examination; Heart muscle.—Interventricular septum. Sections showed that many of the muscle fibres had lost their striations and become homogeneous. Some of them showed the presence of vacuoles. Very rarely a fatty, degenerated fibre was found. In the connective tissue, and about the blood vessels, and to a slight extent in the muscular tissue there were occasional areas of infiltration with small, round, lymphoid cells.

The next cases are of measles and diphtheria, complicated by noma in case twenty-four.

Case XXIII.—Boy, age ten months. Child had been ill with measles, and was admitted to the hospital with diph-

theria, still having the measles eruption. Four days after entrance he developed pneumonia, became pale and cyanotic, and died on the next day.

Autopsy. — March 2, 1897. Legs, arms, chest, neck, and lower portion of face covered with a discrete raised hyperemic papular eruption. *Heart:* weight, 50 grammes. Valves and cavities normal. Heart muscle rather pale. *Tongue*, *tonsils*, *larynx*, *pharynx*, and *trachea* showed no changes except a slight hyperemia of the trachea. *Anatomical diagnosis:* acute broncho-pneumonia of both lungs, with complete consolidation of lower lobe of left lung, chronic tuberculosis of middle lobe of right lung, cloudy swelling of liver, spleen and kidneys, acute lymphatic hyperplasia, papular rash, evidently that of measles, decubitus over sacrum, hyperemia of trachea, acute splenitis. *Cultures:* trachea, many Klebs-Loeffler bacilli, staphylococcus albus; right lung, and left lung, lower lobe, Klebs-Loeffler baccillus, staphylococcus albus and streptococcus; liver, streptococcus (large); spleen, Klebs-Loeffler bacillus and streptococcus; kidney, few Klebs-Loeffler bacilli and colon bacillus.

Microscopical examination; Pneumogastric nerve.—Sections stained by Marchi's method showed both in cross and longitudinal sections extensive degenerative changes, though not exceedingly intense. Almost all the nerve fibres showed the presence of fat, but in rather moderate amount, and confined chiefly to the medullary sheath, which was fragmented and swollen. The axis cylinders were grayish in color in many instances, and swollen and beaded.

Case XXIV. — Boy, age two years. Was admitted to the hospital. Diphtheria bacilli were found in the nose. There was no rash of scarlet fever. He developed broncho-pneumonia, and a gangrene of the face and jaw, and died on the thirtieth day of the disease.

Autopsy.— March 7, 1897. Clinical diagnosis, measles and broncho-pneumonia. All the soft tissues of the posterior pharynx, posterior nares and mouth were covered with a dirty, blackish, soft tissue, hardly firm enough to be called a membrane. *Larynx* and *epiglottis* showed the same accumulation, but no distinct membrane. *Trachea* normal, but slightly congested. *Brain:* weight, 910 grammes,

normal. *Heart:* weight, 50 grammes. Valves and cavities normal. *Anatomical diagnosis:* acute, rapidly spreading necrosis of soft tissues of upper and lower jaw and cheek, with necrosis of the inferior and superior maxillary bones at the margin, and with necrosis of turbinate bones and vomer, necrosis of the soft tissues of the nose, palate, pharynx, uvula and tonsils, purulent fluid in the antrum of Highmore, acute suppurative inflammation of the left middle ear, and mastoid process, acute purulent bronchitis and purulent broncho-pneumonia of both lungs, acute general lymphatic hyperplasia, acute splenitis, acute parenchymatous degeneration of liver and kidneys. *Cultures;* necrotic areas of soft tissues of upper jaw and lower lip showed a variety of organisms among which were streptococci, staphylococcus albus, colon bacillus, and a few Klebs-Loeffler bacilli. The trachea showed a variety of organisms, few streptococci, staphylococcus aureus, but no Klebs-Loeffler bacilli; right lung, lower lobe, few streptococci, and a very few Klebs-Loeffler bacilli; right lung, middle lobe, many streptococci, few Klebs-Loeffler bacilli; left lung, lower lobe, negative; liver, few Klebs-Loeffler bacilli and colon bacillus; spleen, very few Klebs-Loeffler bacilli; kidney, colon bacillus; right middle ear, few Klebs-Loeffler bacilli, and staphylococcus pyogenes aureus; left middle ear, negative. Cover glass preparations from the pus of the lung showed pus cells, streptococci and a few short bacilli.

Microscopical examination; Pneumogastric nerve. — In the sections of this nerve there were very marked and extensive degenerative changes. The nerve fibres were much swollen and beaded, most of them showed the presence of a large amount of fat, and others were granular and grayish in color. Very few fibres seemed normal except for a short distance. The axis cylinders were beaded, broken and replaced by fat drops.

The last case is one of sudden death in pneumonia, in which the pneumogastric nerve was examined. This was not a case of diphtheria.

Case XXV. — Boy, age eleven months. Child was admitted to the hospital with pneumonia. He was reported to have had eleven convulsions the day of entrance, which was the

first day of the disease. On the ninth day it was noticed only that he seemed restless. Died suddenly.

Autopsy.— Feb. 22, 1897. *Heart:* weight, 65 grammes. Valves and cavities normal. *Left lung:* the lower lobe somewhat firmer than the rest of the lung, of a reddish appearance. Muco-purulent material could be squeezed from the bronchi. *Right lung* normal. *Brain:* beneath the pia there was a well marked collection of fluid, the pia being raised from the surface of the brain about 0.8 cm. This was more marked on the left side. Brain otherwise was normal. *Trachea* and œsophagus normal. *Anatomical diagnosis:* last stages of gray hepatization of lower lobe of left lung, edema of brain, acute parenchymatous degeneration of the liver and kidney, acute splenitis, acute general hyperplasia of lymph glands. *Cultures:* heart blood, lower lobe of left lung, liver, spleen and kidneys, sterile.

Microscopical examination; Pneumogastric nerve. Sections varied somewhat. In some nerve bundles scarcely a single normal nerve fibre could be seen. In others the degenerated fibres were approximately one-fourth of all the fibres. The degeneration was marked. There was much fat present in the medullary sheaths and in the axis cylinders, and the other fibres were grayish, swollen, granular and beaded.

The specimens from the above cases were treated by Marchi's method. Other sections were stained by hematoxylin and eosin, and in some of the cases with eosin and Unna's alkaline methylene-blue stain.

Before taking up the discussion of the changes found in the nervous system in diphtheria, let us first see what has been found in the heart muscle in these cases of sudden death from heart failure during infectious diseases.

Oertel, Mosler, Leyden, and Birch-Hirschfeld have described degenerative changes in the heart muscle.

Leyden found fatty changes in the muscle fibre and increase of the nuclei in the muscular tissue, infiltrations about the blood vessels, and in two of his three cases areas of myocarditis. The vagus nerve examined in the third case was normal.

Rosenbach described waxy and granular degeneration of the muscle fibres, and also the presence of lymphoid cells,

and infiltrations about the vessels, and in the interstitial tissue.

Unruh describes myocarditis in localized areas, and fatty changes of the heart muscle, and argues that in these cases, the heart failure does not arise from changes in the nerves, because this is an early symptom, while those, with the paralysis produced by them, appear later. He asks why the nerve to the heart alone should be affected thus early, and not other nerves. He also argues that the cause is muscular because of the dilatation.

Huguenin found granular and hyaline degeneration of the muscle fibres, increase of connective tissue, and much increase of the nuclei with small hemorrhages. He speaks of parenchymatous and interstitial myocarditis, and endarteritis proliferans. The pneumogastric nerve, and medulla he found normal.

Schemm describes fatty and granular degeneration of the heart muscle fibres with swelling and increase of the nuclei, and a slight hyaline degeneration and atrophy. He states that the connective tissue was often somewhat rich in cells, and in one case he found extravasations of blood.

Arnheim found only slight changes in the heart. In three out of eight cases there was cloudiness of a few of the muscle fibres, with no fatty degeneration and no areas of myocarditis. In one other case he states that there was myocarditis, the muscle in general being cloudy.

Rabot and Philippe describe granular degeneration of the muscular fibres of the heart, with a slight increase of the nuclei, and with small areas of inflammatory infiltration with lymphoid and connective tissue cells, and some perivascular infiltration. They found no changes either in the peripheral nerves, or in the central nervous system, and conclude that the essential process in the heart is an interstitial one.

Romberg, in an important paper on the changes in the heart in various infectious diseases, reports eight cases of diphtheria. In these hearts he found albuminoid granulation of the muscle five times; marked once, moderate four times; fatty degeneration five times, always marked; hyaline, or waxy degeneration, was noted as present twice. He also found vacuolization, and enlargement and pigmentation of the nuclei.

He found, moreover, in all eight cases, interstitial alterations, an infiltration of the connective tissue. The amount of infiltration varied, as did also its extent. He found, too, periarteritis, and rarely an infiltration about the ganglion cells of the heart. Hemorrhage was rare. In the eight cases he found myocarditis, marked twice, moderate twice, and slight four times; pericarditis, marked once, moderate twice, slight twice, and absent three times; endocarditis, marked three times, and absent five times.

Welch and Flexner speak of finding more or less intense fatty degeneration of the heart muscle with fragmentation of the nuclei of the muscle fibres.

Hesse found parenchymatous degeneration of the heart muscle, shown by the loss of the striations, cloudiness, vacuolization and the presence of fat. He also describes infiltrations with round cells of the interstitial tissue and about the vessels, as well as hemorrhages. He examined twenty-nine cases. He says that the poisons of infectious diseases produce in all organs parenchymatous degenerations, but in addition alterations of the vessels play an important part. The latter are especially important, and may find their expression either in abnormal hyperemia, a weakening of the vessel wall which leads to hemorrhage, or in an abnormal permeability for round cells, which leads to cell infiltration. In the heart muscle he thinks the most important factors are the dilatation of the small vessels, the hemorrhages and the perivascular infiltrations; but concludes that the heart failure in these cases of sudden death in diphtheria is due to poisoning of the heart.

Preisz, in one case of death from heart failure in diphtheria found that the muscle fibres of the heart had lost their striations, and were granular; while the nerve cells, stained by Nissl's method, showed no changes.

Mollard and Regaud, in a series of experiments upon animals with the toxines of diphtheria, found in the hearts parenchymatous degeneration, as shown by loss of the striations of the muscle fibres, the formation of vacuoles, exudations from the muscle, and fatty degeneration, while the nuclei were swollen and vesicular. They considered the changes in the connective tissue to be secondary, and state that they found only

an infiltration of leucocytes. They also describe degenerations of the muscle fibres of the vessel walls, and infiltration of the walls. They state that in acute and sub-acute cases they found no hyperplasia of the connective tissue elements. They regard the infiltrations which they found as consisting of leucocytes, and state that this is secondary, evidently looking upon the process as one of repair, and the cells as phagocytic. They state that the amount of change found varied in the different individuals, and in parts of the same heart, a fact also mentioned by others.

Vincent examined a case of sudden death in diphtheria in which the fibres of the heart muscle showed no changes except a loss of striation. There was also an increase of the nuclei of the sarcolemma, and about the blood vessels the "connective tissue cells were increased." The blood vessels were dilated. In the medulla the vessels were dilated, but there was no infiltration or hemorrhage, and no changes in the nerve cells. In the pneumogastric nerve the myelin sheath was thickened in places but there was no marked degeneration. The sympathetic nerve was normal. In the lower cervical sympathetic ganglia some of the cells showed granular degeneration. In the cardiac plexus he found marked changes. There was intense parenchymatous degeneration and absence of the axis cylinder. The capillaries were dilated, and the nerve cells were granular, vacuolated, and in some of them there was loss of the nucleus and nucleolus.

Thus we see that the changes in the heart in this disease vary somewhat in character and amount. Of the significance of the changes, we shall have more to say.

Among the earlier writers on the changes in the nervous system in diphtheria is Dejerine. He found in 1878 a degenerative atrophy, characterized by increase of nuclei, fragmentation of the myelin sheaths in the anterior nerve roots, while the posterior roots did not seem changed. In the anterior horns of the gray matter of the cord, he found fewer nerve cells than normal, and some atrophied cells, dilatation of the vessels, and increase of the neuroglia. The white substance was normal. He concluded that there was a parenchymatous neuritis, no changes in the posterior roots, and an inflamma-

tory process in the gray matter, though he states that he did not find vacuolated and swollen cells as he did in myelitis

Leyden in 1880 described the changes of a parenchymatous neuritis with excellent drawings, though not with especial reference to diphtheria.

P. Meyer, in the following year, examining the nervous structures in diphtheria, described extensive, parenchymatous degeneration of the nerves, and slight changes in the nerve cells, consisting in an absence of the cell processes and poorly staining nuclei. The white matter was normal.

Arnheim, besides the changes in the heart muscle spoken of above, found cloudiness of the diaphragm and skeletal muscles. He found in all the nerves examined an extensive degeneration as described by Eichhorst, Leyden and Meyer. The perineurium and endoneurium were without changes. In most of the nerves there was a hyperemia of the nerve sheaths and of the endoneural vessels. In one case he found extensive capillary hemorrhages, both in the nerves and in the cord. In the latter they were almost exclusively in the neighborhood of the vessels of the gray substance, and at times close to the cells of the anterior horn. In the other cases he sometimes found hyperemia and hemorrhages in the peripheral nerves. The ganglion cells were normal. The cells of the vagus nucleus were normal. There were no changes in the white matter of the cord, or in the medulla. He sums up the changes found: as 1, hyperemia and capillary hemorrhages in the peripheral nerves and cord; 2, slight inflammatory changes in the muscles; 3, marked parenchymatous and interstitial degeneration of nerve fibres; 4, negative results in nerve cells; 5, no systemic disease of the cord.

Hochhaus describes parenchymatous clouding of the muscles, most marked in the paralyzed muscles, less in the paretic ones. In the nerves he describes only slight interstitial changes, with increase of the nuclei, and dilatation of the vessels. The brain and spinal cord were normal. We can however neglect his statements as most of the nerves were examined only when fresh, in salt solution, and only a few, and those fresh, in osmic acid.

Bikeles, examining the spinal cord by Marchi's method, found degeneration in the posterior columns, and in the pos-

terior nerve roots, and thinks he has found in this fact an explanation of the ataxia often seen in diphtheritic paralysis.

Cavazzani found more marked changes in the central nervous system. He describes, in infectious processes, a degeneration of the nerve cells with changes in the nuclei, such as vacuolization and atrophy.

Preisz, in speaking of the changes in the nervous system in diphtheria, describes a degeneration of the peripheral nerves and of the vagus, and in the cord microscopical hemorrhages, chiefly in the gray matter, and degenerative changes of some of the ganglion cells of the anterior horn. The white substance was normal, except in his second case, where he found quite a marked degeneration of the posterior columns of the cord.

Of experimental work upon the nerve lesions in diphtheria the most important is that of Babes, Martin, Enriquez and Hallion, and Crocq.

Babes states that in the cord and brain, besides hyperemia, general edema and slight softening, there could be made out numerous irregular diffuse red, softened areas. These were especially well marked in the lateral and posterior columns of the cord.

Martin found degenerations of the nerves in animals after repeated small doses of the toxines of diphtheria, and also after a single large dose. He describes a parenchymatous degeneration of the nerve fibres. The sheath of Schwann is affected first, becoming granular, and later breaking up, while the axis cylinder is affected later, first becoming attenuated at some point, and then breaking at this point, and disappearing beyond. He also states that different branches of the same nerve are often affected to a very different degree, and even the same fibre differently at different points. He found this process affecting the sensory nerves to the same extent as the motor ones. The sympathetic nerve was also affected. He found degenerations in the muscles, and states that this was "proportional to the degree of nerve change." The spinal ganglia, the cord, medulla and brain were found normal in all cases.

Enriquez and Hallion describe, as the result of experiments upon dogs, a vascular dilatation in the gray matter of

the cord, with hemorrhages and myelitis, and myelitis of the white substance. There was also increase of the neuroglia, nerve fibres in various stages of destruction, granular nerve cells, and dilated capillaries. In addition, there was a parenchymatous degeneration of the nerve roots. They think this was a myelitis of vascular origin.

Crocq, experimenting upon rabbits, describes the changes produced in the nerves, as a granular condition, fragmentation and fatty degeneration of the myelin sheaths, and disappearance of the axis cylinder, with multiplication of the nuclei. This he found most marked in the anterior roots, and slight in the posterior ones. He also describes changes in the spinal cord. The nerve cells were swollen and stained poorly; the nuclei and processes had disappeared; there was proliferation of the neuroglia and atrophy of nerve cells, many of which had disappeared, and been replaced by sclerotic tissue. The white matter was only exceptionally altered. In the medulla there was tumifaction of the cells in the lower part, while in the upper part they had remained normal. The cranial nerves were unaffected.

The cases reported in this paper were mostly cases of diphtheria, although a few cases of mixed infection and one of pneumonia have been added, as the nervous changes of one infectious disease are similar to those of others, varying more in degree, or in the liability to affect the nervous system, than in kind. The examinations again were not complete as to all parts of the nervous system except in a few cases, and the chief object of these examinations was to discover whether recent acute degeneration resulting in the breaking down of nerve structures into fat had taken place, and more especially in the peripheral nerves. In spite of the fragmentary character of the work, certain general conclusions seem warranted even at this point.

One of these is that the chief change of the nervous system in diphtheria is an acute degenerative process, chiefly parenchymatous, most marked in the peripheral nerves, affecting both the motor and sensory nerves. The myelin sheath is affected first, and later also the axis cylinder, generally without infiltration, or much multiplication of the nuclei. In this, our results correspond pretty closely with

those of other investigators, both clinical and experimental, as Preisz, Martin and Crocq, as well as earlier observers, such as Mendel, Leyden and others. Nor do these results stand at marked variance with those authors who have found changes in the central nervous system, though hemorrhages and myelitis were not found, yet dilatation of the capillaries was observed, and the more marked changes certainly seem possible, though probably rare. The most marked change found in the central nervous system, and that in the brain, as well as the cord, was the presence of fat here, showing that the effect of the toxic substances upon the nerve structures is not confined to the peripheral nerves. These degenerations were diffuse, but, if anything, more marked in the posterior columns of the cord, as has been noted also by Bikeles; a fact difficult of interpretation unless we assume a less power of resistance to injurious influences in these nerve fibres than is found in others. Indications of the existence of such a fact are not wanting, as shown by the large number of diseases in which degenerative processes have been observed in this region, as for example in pernicious anemia, pellagra, leprosy and others. Perhaps this affection of the posterior columns may account, as Bikeles suggests, for the ataxia so often observed in diphtheritic paralysis. That the cranial nerves do not always escape the process affecting the nervous system so widely is also certain, as shown by the marked degeneration of the fifth nerve found in one case. These results agree with those of Martin, in that the posterior nerve roots were found fully as much affected as the anterior ones. In regard to the condition of the nerve cells one is not warranted in drawing any very definite conclusions from the results obtained by means of the stains used, but certainly there was no myelitis present, and no condition resembling anterior poliomyelitis such as Dejerine thought he had discovered. It seems quite probable, however, that some of the nerve cells would show changes, at least in their finer structure, where the nerve processes have suffered so widely.

The processes found in the specimens of heart muscle examined correspond closely to those previously reported by others. There was a parenchymatous degeneration of the

muscle fibres, shown by loss of the striations, vacuolization, and fatty degeneration. An increase of the muscle nuclei was not present, though the nuclei were quite numerous, but this is due to the fact that the hearts examined were from children in whom, from the small size of the fibres, the nuclei appear to be more numerous. The nuclei showed no marked degenerative changes. The dilatation of the vessels was marked, and also the infiltration, both in the myocardium and in the interstitial tissue. This infiltration consisted mostly of small round lymphoid cells, with a few larger cells, the nature of which could not be accurately determined, because of the methods of hardening used, formol, and Müller's fluid. Certainly leucocytes played no important part in the process, contrary to the statements of Mollard and Regaud. Again, in agreement with other observers, these changes showed considerable variation in the different cases. The most constant was the interstitial process. The fact that changes were found, more or less marked, in all the pneumogastric nerves examined, seems to point to considerable influence upon the mode of death in the cases of sudden death. The objection of Unruh that this accident is an early one, and the paralysis a late one, does not hold, when we remember that sudden death may occur late in the disease, and the paralysis sometimes appear early, as was seen quite frequently in the cases reported in this paper. The view of Hesse, that the heart failure results from the effects of the poison of the disease upon the heart, rather than as a result either of the muscle or of the nerve degeneration, seems nearer the truth. We must ask, however, in what way the poison acts. It seems most probable that in such cases it acts through the nerve structures, interfering with their normal function, and that this may occur before degenerative processes have proceeded far, does not lessen in any way the importance of their occurrence, but would rather lead us to place greater weight upon slight changes, where other obvious causes of death, as markedly degenerated heart muscle, do not exist. The variability of the amount of changes, both in the heart muscle and in the nerves, may point to a varying cause for these cases of sudden death, but the argument in favor of the disturbance of the functions of the nerve seem strongest.

To sum up, the changes in the nervous system produced by diphtheria are; 1, a marked parenchymatous degeneration of the peripheral nerves, sometimes accompanied by an interstitial process, and hyperemia and hemorrhages; 2, acute diffuse parenchymatous degenerations of the nerve fibres of the cord and brain; 3, no changes, or but slight ones in the nerve cells; 4, acute parenchymatous and interstitial changes in the muscles, especially the heart muscle; 5, occasional hyperemia, or infiltration, or hemorrhage in the brain or cord, in rare cases severe enough to produce permanent troubles, such as the cases of multiple sclerosis and of hemiplegia which have been observed. Finally, the probability that the cases of sudden death from heart failure in diphtheria during the disease, or convalescence, are due to the effects of the toxic substances produced in the disease upon the nerve structures of the heart.

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IV.

THE GENERAL INFECTIONS AND COMPLICATIONS OF DIPHTHERIA AND SCARLET FEVER. A BACTERIOLOGICAL STUDY OF ONE HUNDRED AND FIFTY-SEVEN CASES.

Richard Mills Pearce, M.D.,
First Assistant in Pathology, Boston City Hospital.

This paper is a report of the bacteriological examinations of 157 cases of diphtheria and scarlet fever which have been examined post-mortem at the South Department of the Boston City Hospital between February 1 and December 7, 1897. This does not include all the cases from the department, on which post-mortem examinations have been made; but only those of diphtheria in which an absolute diagnosis has been made both clinically and bacteriologically; and only those of scarlet fever in which the clinical diagnosis was perfectly clear. The clinical consideration of these cases is included among those reported by Dr. J. H. McCollom in this number of the *Hospital Reports.*

A report of the macroscopical and microscopical appearances is now being prepared by Drs. W. T. Councilman and F. B. Mallory.

A study of these cases has been made with two objects in view. First, to determine the frequency and nature of the general infection, particularly that with the Klebs-Loeffler bacillus; secondly, to determine the bacterial nature of the complications, particularly broncho-pneumonia and affections of the middle ear. For a study of this nature, a large number of cases, such as we have here, is of much greater value in forming conclusions than a small number of picked cases. These cases have been taken in order, without dropping unimportant ones. In this way I hope to be able to show the bacteriological side of the average cases of diphtheria and

scarlet fever in hospital wards. I am well aware that, in some cases, certain details in examination are lacking, particularly as regards inoculation tests; but I can excuse myself only on the ground that in the routine laboratory work of a large hospital the finer details of the work cannot always be carried out with that perfect regard for scientific accuracy which could be desired. The diagnosis of the various organisms has been based on morphological and cultural characteristics and, in cases where the organisms have occurred in unusual locations, on examination of stained sections. Loeffler's blood-serum has been used as the routine culture medium, with other special media, when necessary for purposes of differentiation. For studying the organisms in tissues, Unna's Alkaline Methylen Blue, preceded by Aqueous Eosin as a contrast stain, has been used.

The work has been done at the suggestion and under the direction of Prof. W. T. Councilman, in the pathological laboratory of the Boston City Hospital.

There have been examined in all 157 cases, which have been divided according to the clinical diagnosis into three groups.

I. Diphtheria, ninety-four cases.

II. Diphtheria, complicated by other infectious diseases, forty-six cases (by scarlet fever in twenty-nine, by measles in eleven, and by both scarlet fever and measles in five).

III. Scarlet fever, seventeen cases (in three of which measles was also present).

These will be spoken of as groups I., II. and III., respectively; and they will be taken up in the order mentioned, the general infection being considered first, and then the complications. Groups I. and II. on account of the frequency in which the Klebs-Loeffler bacillus occurs in both, will be considered together, although the results of the examinations in each group will be stated separately.

General infections in Groups I. and II.

Frosch[1] was the first observer to note, in a series of cases, the occurrence of the Klebs-Loeffler bacillus in the internal organs (heart's blood, liver, spleen, kidney and lymph glands). In 1893, he reported that he had found it in ten out of fifteen cases examined. Kolisko and Paltauf[2] had

previously, however, noted its occurrence in the spleen in one case, as had also Schmorl,[3] in the cervical lymph glands, in seven out of ten cases. Booker,[4] in one case, found it in the spleen, lung, submaxillary gland and heart's blood. Kutscher[5] found it, in one case, in the liver and kidney, and in the lung in eight out of nine cases. Canon[6] found it repeatedly in his post-mortem examinations. Kanthack and Stephens[7] found it in the lung in each of twenty-six cases, in the spleen in ten of twenty-one cases, and in the kidney in two of three cases. Wright[8] in fourteen cases demonstrated it in the lung thirteen times, in the liver three times, in the spleen twice, in the cervical and bronchial glands five times, in the mesenteric glands twice, in the heart's blood once, and in the kidney once. In seven of these cases there was also a general streptococcus infection. Wright and Stokes[9] in a later series of cases, which probably included Wright's first series, reported thirty-one cases, in which the Klebs-Loeffler bacillus was found in the lungs thirty times, in the liver nine times, in the mesenteric glands seven times, in the spleen and the heart's blood each five times, in the cervical glands four times, in the brain and bronchial glands each twice. The streptococcus was present in twenty cases, and the pneumococcus or staphylococcus pyogenes aureus in five cases. Stokes,[10] in nine cases, treated by antitoxin, found it in the lungs nine times, in the kidney four times, in the heart's blood and spleen, each once. Within the last year and a half, Nowack[11] reports twenty-two fatal cases in twenty-one of which the streptococcus was found in the internal organs. In nine of these it was associated with the Klebs-Loeffler bacillus; and in one, with a bacillus resembling it except in virulence. Genersisch[12] in the examination of twenty-five cases of "septic" diphtheria did not always find the streptococcus present in the blood or internal organs, and thinks that the Klebs-Loeffler bacillus alone can produce the so-called "septic" symptoms. Reiche[13] in examining forty-two fatal cases found streptococci and staphylococci in 64.3 per cent., streptococci alone in 45.2 per cent., and the Klebs-Loeffler bacillus alone twice. Stephens and Parfitt[14] report three fatal cases, one with a general infection with the Klebs-Loeffler bacillus and the streptococcus, and a second with the

Klebs-Loeffler bacillus only, and a third with the pneumococcus. In the second case the bacilli were demonstrated in cultures from the blood during life. Flexner[15] has demonstrated a general infection with the bacillus of diphtheria in one case. Babes[46] has done the same. Dahmer[47] reports finding the streptococcus in the blood of diphtheria in 50 per cent. of the cases which he examined. In 36 cases, he found it in both the heart's blood and spleen 17 times, and in the lungs (with or without broncho-pneumonia) 30 times. In 10 of the latter it was associated with staphylococci. He kept no record of the occurrence of the Klebs-Loeffler bacillus.

In inoculation experiments with guinea-pigs Wright[9] found the Klebs-Loeffler bacillus nineteen times in 155 livers, fifteen times in 152 spleens, four times in 151 kidneys, seven times in the blood of 153 hearts. Abbot & Ghriskey[16] found that by inoculating the testes of rabbits with Klebs-Loeffler bacilli, small bodies made up of leucocytes and Klebs-Loeffler bacilli were found in the omentum. Zarniko,[17] in a few cases, found Klebs-Loeffler bacilli in the necrotic foci of the livers of inoculated animals.

Of the ninety-four cases of group I, the *heart's blood* in four showed the presence of the Klebs-Loeffler bacillus, twice alone and twice with the streptococcus. In nine cases the streptococcus occurred alone. In one case the pneumococcus occurred alone.

In the *liver*, the Klebs-Loeffler bacillus occurred in twenty-four cases, alone in twelve cases and with the streptococcus in twelve cases. The streptococcus occurred in twenty-seven cases, alone in fourteen, with the Klebs-Loeffler bacillus in twelve, and with the staphylococcus pyogenes aureus in one case. The staphylococcus pyogenes aureus occurred in four cases, alone in three cases and associated with the streptococcus in one case. The pneumococcus occurred alone once.

In the *spleen*, the Klebs-Loeffler bacillus occurred in eighteen cases, in fifteen of which it was the only micro-organism present, and in three associated with the streptococcus. The streptococcus occurred in twenty-four cases, alone in twenty-one, associated with the Klebs-Loeffler bacillus twice, and with the staphylococcus pyogenes aureus once. The

staphylococcus pyogenes aureus occurred twice, once alone and once with the streptococcus. The pneumococcus occurred alone twice.

In the *kidney*, the Klebs-Loeffler bacillus occurred in twenty-three cases, in fifteen of which it was alone, in five associated with the streptococcus, and in two with the staphylococcus pyogenes aureus. The streptococcus occurred in twenty-six cases, in nineteen of which it was the only organism present. The staphylococcus pyogenes aureus occurred in eight cases, in four of which it was in pure culture. The pneumococcus occurred four times, three times in pure culture and once with the Klebs-Loeffler bacillus.

In group II. (forty-six cases) the *heart's blood* showed the presence of the streptococcus in pure culture nine times, and associated with the Klebs-Loeffler bacillus once. The Klebs-Loeffler bacillus occurred alone once.

The *liver* in twenty-five cases showed the presence of organisms. The streptococcus occurred alone ten times, with the Klebs-Loeffler bacillus seven times and with the staphylococcus pyogenes aureus three times. The Klebs-Loeffler bacillus occurred in pure culture five times.

The *spleen* showed the presence of organisms in twenty cases. The streptococcus occurred alone thirteen times, and with the Klebs-Loeffler bacillus twice. The latter was present in pure culture five times.

The *kidney*, in twenty-nine cases in which organisms were present, showed the presence of the streptococcus in pure culture ten times, associated with the Klebs-Loeffler bacillus five times, and with the staphylococcus pyogenes aureus three times. The Klebs-Loeffler bacillus occurred alone seven times. The staphylococcus pyogenes aureus and the pneumococcus each occurred alone once, and together once.

It is of interest that, in both these series, the kidney had the greater number and variety of organisms.

References to the general infection in cases like those of the second group are not numerous. Wright[8] reports eleven cases, in which there was a general infection with the streptococcus in four, and with the pneumococcus in one.

In taking cultures from these organs, the amount of material used to inoculate the culture tubes was that which

would adhere to the sides of a sterilized, flattened, platinum wire thrust into their substance; the surface of the organs being first seared with a heated spatula. In the case of the heart's blood, the needle was thrust into the latter portion of the blood as it escaped from the right auricle after cutting the inferior vena cava. Thus it will be seen that a comparatively small amount of material was used for inoculation. In most cases, nevertheless, the growth of the Klebs-Loeffler bacillus was fairly abundant, generally from three to fifteen colonies on each tube; but sometimes many more. Thus, in several cases, it was noted that cultures from certain livers showed eighteen, twenty-four, twenty-five and thirty-five colonies respectively. The spleen cultures never showed more than nine colonies. The kidney cultures in two cases showed nineteen and twenty-four colonies respectively. In some cases the growth was only in the water of condensation. This was especially true of the heart's blood, in which in only two of the six cases were there distinct colonies (three) on the surface of the serum; the other four having a growth only in the water of condensation. The results (as regards the amount of the growth) differ from those of most of the observers mentioned above (excepting Kanthack, Stephens and Flexner), in that they considered it necessary to use a large amount of material in order to demonstrate the presence of the bacillus at all. In some of the cultures from these organs involution or degenerate forms were present in considerable numbers.

The significance of this general infection with the Klebs-Loeffler bacillus is not apparent. It occurred generally, but not always, in the gravest cases or those known as "septic" cases. It is probable that it may be due to a diminished resistance of the tissue cells or of the germicidal power of the blood. Whether it has a clinical significance is not apparent. In this series of fatal cases the number of infections with the streptococcus and with the Klebs-Loeffler bacillus were about even, though slightly in favor of the streptococcus.

Whether the Klebs-Loeffler baccillus does or does not continue to produce its toxic products wherever it may be, in the blood or internal organs, it is impossible to say, but from the number of fatal cases with such an infection it would seem

very probable that it does. Kanthack and Stephens[7] incline to this opinion; and, as previously stated, Genersisch[12] considers many of the so called "septic" cases to be due to such an infection, independently of the streptococcus.

In comparing groups I. and II. the general infection appears to be about equal, though slightly greater in group II.; thus group II., with forty-six cases, has about the same percentage of cases with general infection as group I., with ninety-four cases. This is true as regards infections with both the streptococcus and the Klebs-Loeffler bacillus, but as would be expected, the former are more numerous than the latter.

COMPLICATIONS IN GROUPS I. AND II.

Broncho-pneumonia. — The presence of the bacillus of diphtheria in this complication was first noticed by Thaon[18] in 1885, later by Johnson[19] and Martin[46], each in one case. By Strelitz[20] in one out of eight, by Flexner[15] in one out of two, by Mosny[21] in one out of three, by Kutscher[5] in eight out of nine, by Netter[22] in four out of seven cases, and by Frosch.[1] Wright and Stokes[9] found it in eighteen out of nineteen cases, in eight of which it was obtained in pure culture, and in the other five was associated with the streptococcus. Kanthack and Stephens[7] also found it in most of their cases.

Of other organisms associated with this complication the pyogenic cocci are the most common, particularly the streptococcus, according to Thaon,[18] A. Fränkel,[23] Prudden,[24] Neumann,[25] Mosny,[21] Northrup[24] and Wright.[8,9] The pneumococcus has also been found to be often present. Wollstein[45] reports thirty-three cases, occurring in the Babes' Hospital, New York, fourteen of which were secondary to diphtheria, scarlet fever or measles. In eleven of the latter the pneumococcus was found. In two cases it occurred in pure culture and in the others was associated with the streptococcus and staphylococci.

Belfanti[53] reports twenty-six cases complicating diphtheria. In these he found the Klebs-Loeffler bacillus in the lungs in twenty-one cases, in four of which it occurred in pure culture. He found the streptococcus in twenty cases,

staphyloccoccus pyrogenes aureus in ten cases and the pneumococcus in three cases. He concludes that the Klebs-Loeffler bacillus, either alone or associated with other organisms, may cause broncho-pneumonia.

In the first group of cases, broncho-pneumonia was present in sixty. The Klebs-Loeffler bacillus occurred in forty-six and the streptococcus in thirty-three cases. The Klebs-Loeffler bacillus occurred alone in ten cases, and associated with the streptococcus in eleven, with the streptococcus and staphylococcus pyogenes aureus in seven cases, with the latter only in three cases, and with the pneumococcus in four cases. The streptococcus occurred alone in eight cases, with the staphylococcus pyogenes aureus in three, and with the pneumococcus in two. The pneumococcus occurred in eight cases, in two of which it was in pure culture. The staphylococcus pyogenes aureus occurred in eleven cases, but always in connection with other organisms. (Of the fifty-eight cases reported above, fifteen were included in a previous bacteriological report of 128 cases of broncho-pneumonia.*) The presence of the Klebs-Loeffler bacillus in such a large number of cases cannot be due entirely, as is claimed by some observers, to the penetration of small bronchi by the needle while taking cultures, for stained preparations of the lungs in these cases show the bacilli to be present in the exudate in the alveoli in nearly all cases, and often in immense numbers.

The observation that in some cases, both in culture and in histological preparation, the Klebs-Loeffler bacilli are present in much larger numbers than are the pyogenic cocci, and that in 17 per cent. of the cases it occurred in pure culture, would indicate an etiological relation. In a previous report* on this condition it was present in sixty-three out of seventy-three cases, in seventeen of which it was in pure culture. Kanthack[7] and Kutscher[5] both think that a broncho-pneumonia may be due to the Klebs-Loeffler bacillus without the aid of the pyogenic cocci.

In group II. broncho-pneumonia occurred in twenty-four cases. The Klebs-Loeffler bacillus occurred in nineteen

* The Bacteriology of Lobar and Lobular Pneumonia. — Boston Medical and Surgical Journal, Dec. 2, 1897.

cases. In only one case was it found in pure culture In the others it was associated with either the streptococcus or the staphylococcus pyogenes aureus or both. The streptococcus occurred in thirteen cases, in two of which it was the only organism present.

The pneumococcus occurred alone once, and with the bacillus pyocyaneus once. The staphylococcus pyogenes aureus occurred in eleven cases, but always in combination. The albus occurred alone once.

The results in this group differ from those of group I., only in the increased frequency of the presence of the pyogenic cocci; particularly the streptococcus. The observation of most investigators, that broncho-pneumonia in the majority of cases is due to a combination of organisms, most frequently the pyogenic cocci, is supported by the results in both groups.

Empyaema. — Was found in the first group in two cases and a fibrinous pleurisy in one case. The streptococcus was found in both cases of empyaema, in one in pure culture, in the other associated with the Klebs-Loeffler bacillus. The cause of the empyaema in this second case was the rupture of a small abscess near the surface of the lung. This lung showed broncho-pneumonia with multiple small abscesses from which in cultures the Klebs-Loeffler bacillus and the streptococcus were found. The fibrinous pleuritis was due to the pneumococcus.

In the second group there were two cases of empyaema and two of fibrinous pleuritis. In the first two cases the streptococcus was present in both, in one in pure culture, in the other associated with the Klebs-Loeffler bacillus. In this last case which had been operated upon there was the remains of a small abscess cavity on the surface of the lung. The two cases of fibrinous exudate showed pneumococcus in one and the pneumococcus and streptococcus in the other.

The only reference that I can find in regard to the occurrence of the Klebs-Loeffler bacillus in the above condition is that of Frosch.[1] He found it not only in the pleural but also in the pericardial exudate. The organisms most commonly found are the streptococcus, pneumococcus and less often the staphylococcus pyogenes aureus.

Abscess of the lung, occurred in three cases of the first group. In one case, the Klebs-Loeffler bacillus and the streptococcus were found, in a second the Klebs-Loeffler bacillus and the staphylococcus pyogenes aureus, and in a third the streptococcus with the staphylococci pyogenes aureus and albus. This first case corresponds to the second case of empyaema in group I.

In the second group, abscess of the lung occurred in two cases. In one the streptococcus was found, and in the other the streptococcus and the Klebs-Loeffler bacillus. This last case corresponds to the second case of empyaema in group II.

Acute Pericarditis, occurred not at all in the first, and three times in the second group. In two of the latter the pneumococcus was found and in one the streptococcus.

Acute ulcerative endocarditis.—But two cases of endocarditis, in which the Klebs-Loeffler bacillus has been found in the vegetations, are on record. The first was that of Howard[26] who cultivated from the valvular vegetations in the heart and from infarcts in spleen and in kidney, a bacillus identical with the Klebs-Loeffler bacillus in everything except virulence. Wright[8] reports a case in which the aortic and tricuspid valves were affected; and in which cultures showed the pneumococcus, staphylococci and a bacillus corresponding to the Klebs-Loeffler bacillus, except that it was non-pathogenic for guinea-pigs.

In the first group there was one case of endocarditis from which the streptococcus was obtained in pure culture. In this case there existed a general streptococcus infection.

In one case of the second group, on the mitral curtain, was a reddish gray, soft, clot-like mass, firmly adherent to the free edge of the valve. Cultures from this mass showed a pure growth of the Klebs-Loeffler bacillus. Sections of the vegetation showed fibrin with pus and coagulated material, with here and there single bacilli, which resembled those of diphtheria, but no clumps of bacilli. There were also a few cocci in indefinite arrangement. This was a case of scarlet fever, with diphtheritic rhinitis, tonsillitis and laryngitis, with broncho-pneumonia of both lungs, and marked general lymphatic hyperplasia, in a child two years old. The Klebs-

Loeffler bacillus was present in the heart's blood, liver, spleen and kidney.

Inflammation of the middle ear, with or without involvement of the mastoid cells, occurred in thirty-two cases of the first group. In eighteen cases it was bilateral, and in fifteen unilateral. In the double cases, the Klebs-Loeffler bacillus occurred in both ears in sixteen cases. In no case did it occur in pure culture in both ears. In three of the sixteen cases it was present in pure culture in one ear; while the other ear in two cases had the staphylococcus pyogenes aureus, and in the third, an unknown diplo-bacillus. In five cases it was associated with the staphylococcus pyogenes aureus, in one with the streptococcus, and in one with the pneumococcus in both ears. In the other five cases it was associated with various combinations of the above organisms. In the seventeenth case it was associated with the streptococcus and the staphylococcus pyogenes aureus in one ear and in the other ear with the former only. In the eighteenth case the streptococcus occurred alone in both ears.

In the fifteen single cases, the Klebs-Loeffler bacillus occurred nine times. It occurred twice in pure culture, with the streptococcus twice, with the staphylococcus pyogenes aureus twice, and in the other three cases with various combinations of these organisms. Of the remaining six cases, in four the streptococcus was present in pure culture; and in the other two the staphylococci aureus and albus occurred.

In the second group the middle ear was involved in twenty cases. In thirteen the affection was bilateral, and in seven unilateral. In the bilateral cases the Klebs-Loeffler bacillus occurred eleven times in both ears. It occurred alone once, with the streptococcus twice, and in the other cases with various combinations of the streptococcus and the staphylococci aureus and albus. The bacillus pyocyaenus was present in two cases. Of the two cases, without the Klebs-Loeffler bacillus, the streptococcus was present in both cases, in one case being associated with the staphylococcus pyogenes aureus in one ear. Of the seven single cases the Klebs-Loeffler bacillus occurred in three. It was present alone once, and with the staphylococcus pyogenes aureus twice. The streptococcus was present in the other four cases.

It is not to be understood that in the above cases the organisms mentioned were the only ones present. In some cases various non-pathogenic organisms were associated with those known to be pathogenic. Several of these were isolated and studied, but none showed pathogenic properties when inoculated into guinea-pigs or rabbits. The presence of these organisms is readily explained by the easy communication with the mouth through the Eustachian tube. This also explains the frequency of the presence of the bacillus of diphtheria. The presence of this bacillus, in these cases, in the absence of histological examination demonstrating its relation to the process, is insufficient evidence of an etiological relation. It is of interest that many of these cases showed no clinical evidence of ear trouble.

The presence of the Klebs-Loeffler bacillus, in acute conditions of the middle ear and mastoid, has been noted by Councilman[27] in one case of diphtheria and two of measles (without diphtheria of the throat). Also by Wright[8] in two cases, in one of which the streptococcus was also present; and by Stephens and Parfitt[14] in one case in which the pneumococcus was also present. Lommel[28] reports twenty-five cases of diphtheria, in twenty-four of which there was disease of the middle ear, but in only one was a bacteriological examination made. In this one case the pneumococcus was found. Rimini[48] reports a fatal case of pyaemia the source of infection being a suppuration of the middle ear following diphtheria. "Large numbers of cocci" were found to be present.

Antra of Highmore.— In group I. there was an infection of the antrum on both sides in seven cases. In all these cases the Klebs-Loeffler bacillus was present in the exudate. Twice it was associated on either side with the staphylococcus pyogenes aureus, once with the streptococcus, once with the pneumococcus and once with a variety of non-pathogenic organisms. Twice it occurred alone on one side and associated with the streptococcus and staphylococcus pyogenes aureus respectively on the other. In group II. it occurred twice on both sides, once with the Klebs-Loeffler bacillus and various unknown organisms; and once with the streptococcus and staphylococcus pyogenes aureus.

In the nine cases the presence of a definite false membrane was demonstrated in four, a purulent fluid in four, and a slightly cloudy serous fluid in one. In the last case the Klebs-Loeffler bacillus and the pneumococcus were present. In one case, in which smears were made from the pus, the Klebs-Loeffler bacillus were seen in large numbers, both free and in pus cells. As in the ear, various unrecognized organisms were generally found associated with the known pathogenic organisms.

This infection of the antra may be one of the explanations of the frequent persistence of the bacillus in the nose after all clinical evidence of diphtheria has disappeared, because the antra drain slowly and consequently do not so readily become free of the diphtheria bacilli and other organisms and the exudation produced by them. In the literature to which I have had access I can find no reference to this condition complicating diphtheria. Most writers on disease of the antrum consider "a cold" as the chief etiological factor.

The comparatively large number of cases in which it has been observed in this series is due to the method of examination. After opening the head and removing the brain in the usual way the nasal pharynx and adjoining cavities have been examined by Harke's[29] method. This method is briefly as follows: The original anterior scalp flap is dissected down over the frontal bone to its union with the nasal bones. The posterior flap is also lengthened, by continuing the incision from back of the ears down along the anterior edges of the trapezius muscles to a point below the middle of the back of the neck, on either side. The base of the skull is then sawn through in the median line. Posteriorly the base can be entirely divided by sawing at an angle through the bodies of the first three or four vertebræ. In the anterior fossa the separation is completed by the chisel and hammer. The two halves of the skull are then forcibly separated, after which the sphenoidal and frontal sinuses can be examined readily. The distribution of membrane in the post pharynx and nasal cavities can be studied and the presence or absence of adenoids noted. By chipping away the turbinated bones on either side the antra are exposed, and can be examined with little difficulty. The two halves of the skull can readily be

brought together again and easily united with copper wire. If done with care there is no disfigurement.

This method was not used until the middle of the summer. If it had been followed in all the cases of this series there would have been, undoubtedly, a larger number of infections of the antra to report.

Sphenoidal sinus. — In two cases of the first group a muco purulent fluid was found in this cavity. In one case in which there was a general streptococcus infection this organism was also found in the sphenoidal sinus. In the second case there was a "variety of organisms" with abundant Klebs-Loeffler bacilli, many of which were degenerate forms.

Thrombosis of lateral sinus. — One case of the first group showed the presence of the streptococcus and the Klebs-Loeffler bacillus. This condition was associated with a mastoiditis. There was also a general infection with the same organisms. Councilman[49] reports a case of diphtheria developing in the course of typhoid fever in which there was a purulent infiltration of the sub-maxillary and parotid glands, together with a softened thrombus of the external jugular vein, and embolic foci of suppuration in the lungs. Cultures from the lungs showed the Klebs-Loeffler bacillus and staphylococci. Microscopic examination of the thrombus showed large numbers of the Klebs-Loeffler bacillus and a few cocci. The abscesses in the lungs had developed around small branches of the pulmonary artery and contained the Klebs-Loeffler bacillus in large numbers. There were also emboli of the small branches of the pulmonary arteries, which were composed entirely of the Klebs-Loeffler bacillus.

* *Diphtheritic œsophagitis* occurred in two cases of the first group and *diphtheritic gastritis* in one. In all of these the Klebs-Loeffler bacillus, generally with the streptococcus, was found in culture from deeper layers of the process. In these three cases the bacillus has also been demonstrated in histological preparations. In a case of the second group, in which an anatomical diagnosis of diphtheritic gastritis was made, the specific bacillus was found in cultures from the local

* One case of Group I. and the case mentioned as occurring in Group II. have been previously reported by Dr. T. Leary before the Boston Society of Medical Sciences, June, 1897.

process and from the gastro hepatic lymph glands. Histological examination of this case has not yet been made so that I do not report it as an undoubted case. There were three other cases in these two groups, which anatomically showed a diphtheritic process in the stomach, and in which cultures showed the presence of the Klebs-Loeffler bacillus; but which have not yet been confirmed by histological examination. In all of these cases the diphtheritic process in the respiratory passages was extensive, and in one there was also a general tuberculosis. There was also a general infection either with the streptococcus or with the Klebs-Loeffler bacillus or with both, in each case.

The literature contains several references to diphtheritic processes in the œsophagus and stomach; but I have found only one case, that of Loeffler,[30] in which the bacillus has been demonstrated in section. This method of demonstrating its relation to the process is the only certain one, for the presence of the Klebs-Loeffler bacillus in the stomach as demonstrated by culture is of no significance. In this series, in all cases of diphtheria, in which cultures were taken from the normal stomach the bacillus was always found, generally in considerable numbers.

Diphtheritic conjunctivitis occurred in one case of the second group. The process was bilateral and the Klebs-Loeffler bacillus was present in abundance. Babes[32] was the first observer to demonstrate the presence of the Klebs-Loeffler bacillus in this process. Escherich,[31] Elschig,[33] Kolisko and Paltauf,[2] and Wright[8] have each reported single cases of this complication. Diphtheritic processes of the conjunctivae, even those occurring in the course of true diphtheria of the respiratory passages are not always due to the Klebs-Loeffler bacillus. Flexner[46] reports two cases due to the streptococcus.

Diphtheritic vulvitis and *vaginitis* occurred in one case of the first group. In this case there was extensive diphtheria of the respiratory tract. The Klebs-Loeffler bacillus was present in large numbers in cultures from the membrane.

Diphtheritic dermatitis. — In one case, in which there was eczema of the skin of the external ear and mastoid region, following an irritating discharge of the middle ear which con-

tained the Klebs-Loeffler bacillus, a typical false membrane developed, in which the Klebs-Loeffler bacilli were found in large numbers.

The presence of this bacillus in processes of this nature occurring in the course of diphtheria has been observed in ulcers and abrasions of various parts of the body by Wright[8] in seven cases (one being fistula in ano), by Neisser[34] in one case (around anus), by Brunner[35] in a case of phlegmon of the scrotum and in three inflammatory processes of the fingers, by Spronk[36] in inflammatory tissue around tracheotomy wound (three cases), and by Park[46] in two cases of wound of finger after tracheotomy. Treitel and Abel[46] also report true diphtheritic wound infection. Post[37] has reported one case (in adult) and McCollom[38] two cases (in children), of diphtheria of the penis.

Acute abscesses. — In the first group six were noted. Three of these were of the cervical glands, in two of which were found the Klebs-Loeffler bacillus and the staphylococcus albus. The third was due to the streptococcus and the staphylococcus pyogenes aureus, as was also a retropharyngeal abscess. An abscess of the scalp contained the staphylococcus pyogenes aureus; and one of a bronchial gland the streptococcus.

In the second group ten abscesses were examined. Six were of the cervical glands and in four the streptococcus was found in pure culture. In the other two the Klebs-Loeffler bacillus occurred, in one associated with the streptococcus and in the other with staphylococcus pyogenes aureus. A retro-pharyngeal abscess contained the Klebs-Loeffler bacillus, streptococcus and staphylococcus pyogenes aureus, while a laryngeal abscess contained the streptococcus and the staphylococcus pyogenes albus. An abscess of the spleen with an associated peritonitis was due to the streptococcus as was also an accumulation of pus over the trochanter of the femur.

It is of interest that suppuration occurred most commonly in the cervical glands. According to Henoch[46] suppuration of these glands occurs in 2 per cent. of all cases. In this series of 157 fatal cases it occurred in about 7 per cent.

These abscesses are generally due to the ordinary pyogenic cocci. Sometimes the Klebs-Loeffler bacillus is also present,

as in the abscess of the finger which Wright[8] reports, and that of the larynx reported by M. Koch.[39] Leary[40] reports an abscess of the finger, the result of an autopsy wound from a case of diphtheria, which contained the bacillus of diphtheria in pure culture. According to McCollom,[41] abscesses forming at the point of injection of antitoxin, are generally due to the streptococcus pyogenes.

Acute peritonitis occurred in one case of each group. Both were due to the streptococcus. One was associated with the abscess of the spleen previously mentioned in group II.

Group III. Seventeen cases of scarlet fever (measles also present in three).

General infection. — The occurrence of micrococci in the blood and internal organs of fatal cases of scarlet fever was first observed by Crooke[51] in 1885, in thirty cases. Since then Fränkel and Frendenburg[51] have found streptococci in various organs of three cases, as has also Raskin[51] in the heart's blood in four cases, as well as in suppurating glands and joints. The same observations have been made by Leubartz,[51] Kurth[51] and Babes,[51] the latter finding it constantly in the kidney. Wright,[9] in eleven cases, found a general infection with the streptococcus in four cases, with the pneumococcus in one and a poly-infection with the pus cocci in one case (in two of these diphtheria was also present). Lemoine,[42] in two out of thirty-three cases, found the streptococcus in the blood during life. In the urine in each of twenty-two cases of albuminuria associated with the disease he also demonstrated the same organism; while in eleven non-albuminuric scarlet fever urines he found it only once.

Of the seventeen cases of group III., cultures from both the *heart's blood* and *liver* showed the streptococcus to be present in four cases. In the *spleen* it was found twice and the staphylococcus pyogenes aureus once. In the *kidney* it was found in five cases, in four of which it was in pure culture, and in one it was associated with the staphylococcus pyogenes aureus. In a sixth case the latter organism was present in pure culture.

Broncho-pneumonia was present in nine cases. The streptococcus occured six times, twice in pure culture, and with the staphylococcus pyogenes aureus three times. The latter

occurred alone twice, as did also the pneumococcus. In the ninth case there was a combination of several of these organisms.

Netter[43] reports four cases of broncho-pneumonia, in two of which the streptococcus and pneumococcus occurred. Queissner[44] reports four cases in each of which the pneumococcus was present, either alone or with some of the pus cocci.

Acute pleuritis. — One case was observed in which the organism present was the streptococcus. Lemoine[42] reports two case due to the same organism.

Acute inflammation of the middle ear occurred in four cases, three of these were double and one single. Of the double cases one was due to the staphylococcus pyogenes aureus one to the streptococcus; and in the third the streptococcus occurred in one ear and the pneumococcus in the other. In the unilateral case, the streptococcus was present.

* Netter reports one case of this kind in which the streptococcus was found.

Acute abscess occurred in four cases, two were of the cervical and two were of the mesenteric glands. Of these, three contained the streptococcus, which in one (the mesenteric) was associated with the staphylococcus pyogenes aureus; and the fourth (cervical) contained the latter organism only.

* Netter reports four abscesses, due to the streptococcus, occurring in the course of scarlet fever.

The findings in the above cases, indicate the prominent part which the streptococcus plays in the complications and general infection of scarlet fever. The streptococcus found in group III. as well as in the entire series has been considered as identical with the streptococcus pyogenes. I no case has a streptococcus been found which showed peculiarities of form of growth sufficient to cause it to be considered other that the streptococcus pyogenes.

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*In discussion of Lemoines' paper.

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V.

SEVENTY-ONE CASES OF CEREBRO-SPINAL MENINGITIS.

By Francis H. Williams, M.D.

It is not my intention to consider here the various epidemics of cerebro-spinal meningitis that have occured since 1805 in the United States and other countries, nor the recognition in recent years of a diplococcus as a cause of this serious malady but with the kind permission of the medical staff of the Boston City Hospital, to give an outline of the cases that have entered their services, as well as my own, between January 1, 1897, and December, 1897, seventy-one in all. The records are in many instances incomplete for various reasons; many patients do not speak English or they may be brought to the hospital in an unconscious condition and unaccompanied by friends. The tabulation by localities shows that one part of the city has not been markedly more affected than another. The patients have been youths and adults, as children have been sent to the Children's Hospital. The mortality has been nearly 61 per cent.; forty-nine died; twenty-two recovered.

The disease has been characterized by sudden onset; the most constant symptom has been headache, associated usually with some tenderness to pressure in the neck or pain on movement there or retraction of the neck. Delirium occurred in most of the cases, vomiting was a frequent symptom and strabismus, failure of the pupils to react, nystagmus, diplopia, or optic neuritis have been often noted. The temperature was very irregular, and this want of regularity is quite characteristic of the disease. The pulse in some cases was rapid, in others it was less than normal, and in still others it was slower than the symptoms present would lead one to expect. In nineteen cases there was herpes labialis.

The leucocytes were counted in thirty-two cases, and in twelve of these there were at some period of the disease less than

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Chapter Seventy-Six 1238

Chapter Seventy-Seven 1255

Chapter Seventy-Eight 1271

Chapter Seventy-Nine 1288

Chapter Eighty 1304

Chapter Eighty-One 1321

Chapter Eighty-Two 1337

Chapter Eighty-Three 1354

Chapter Eighty-Four 1370

Chapter Eighty-Five 1387

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Chapter One Hundred Twenty-Eight 2096

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Chapter One Hundred Thirty 2129

Chapter One Hundred Thirty-One 2146

Chapter One Hundred Thirty-Two 2162

Chapter One Hundred Thirty-Three 2179

Chapter One Hundred Thirty-Four 2195

Chapter One Hundred Thirty-Five 2212

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Chapter One Hundred Fifty-Seven 2575

Chapter One Hundred Fifty-Eight 2591

Chapter One Hundred Fifty-Nine 2608

Chapter One Hundred Sixty 2624

Chapter One Hundred Sixty-One 2641

Chapter One Hundred Sixty-Two 2657

Chapter One Hundred Sixty-Three 2674

Chapter One Hundred Sixty-Four 2690

Chapter One Hundred Sixty-Five 2707

Chapter One Hundred Sixty-Six 2723

Chapter One Hundred Sixty-Seven 2740

Chapter One Hundred Sixty-Eight 2756

Chapter One Hundred Sixty-Nine 2773

Chapter One Hundred Seventy 2789

Chapter One Hundred Seventy-One 2806

Chapter One Hundred Seventy-Two 2822

Chapter One Hundred Seventy-Three 2839

Chapter One Hundred Seventy-Four 2855

Chapter One Hundred Seventy-Five 2872

Chapter One Hundred Seventy-Six 2888

Chapter One Hundred Seventy-Seven 2905

Chapter One Hundred Seventy-Eight 2921

Chapter One Hundred Seventy-Nine 2938

Chapter One Hundred Eighty 2954

Chapter One Hundred Eighty-One 2971

Chapter One Hundred Eighty-Two 2987

Chapter One Hundred Eighty-Three 3004

Chapter One Hundred Eighty-Four 3020

Chapter One Hundred Eighty-Five 3037

Chapter One Hundred Eighty-Six 3053

Chapter One Hundred Eighty-Seven 3070

Chapter One Hundred Eighty-Eight 3086

Chapter One Hundred Eighty-Nine 3103

Chapter One Hundred Ninety 3119

Chapter One Hundred Ninety-One 3136

Chapter One Hundred Ninety-Two 3152

Chapter One Hundred Ninety-Three 3169

Chapter One Hundred Ninety-Four 3185

Chapter One Hundred Ninety-Five 3202

Chapter One Hundred Ninety-Six 3218

Chapter One Hundred Ninety-Seven 3235

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10,000; this was true in four of the fatal cases, but a subsequent count in three gave a great increase in numbers; in the fourth there was no subsequent count. If, therefore, the leucocyte count when used in the diagnosis of cerebro-spinal meningitis, gives no leucocytosis, a second count should be made. In thirteen cases, more than one count was made and the subsequent count or counts showed a marked increase in the leucocytes in the six fatal cases (three of these have been alluded to above); in the remaining seven that recovered there was a striking decrease in five, no change in one, and in the seventh the decrease was followed by an increase and this again was succeeded by a diminution. These cases indicate that the leucocyte count may sometimes assist in the prognosis.

The serum test for typhoid fever was tried in ten cases and was positive in one only, that of a negro.

Lumbar puncture was done in forty cases, and judging from these this puncture does no harm and it readily establishes the diagnosis when fluid containing the organisms is found; it is sometimes very serviceable for diagnosis as often there is no history and the symptoms may be few. It should be borne in mind that the bacterial examination may give a negative result even in cerebro-spinal meningitis unless the test is made by those who have had much experience. The operation for lumbar puncture, under strict antiseptic precautions, is readily done by using a small trocar to tap the sac surrounding the spinal cord and drawing off some of the fluid; the point of insertion is between the third and fourth lumbar vertebræ. I have usually chosen a point slightly lower than the lowest part of the spinous process of the second lumbar vertebra, and one inch outside of it, and inserted a small sized trocar, somewhat downward and inward to a depth of rather more than two inches. I have always used a trocar instead of a needle, as the latter is liable to be bent or broken off, and is too small to allow the thick pus that is present in some cases to flow through it easily.

The present treatment of the disease is wholly unsatisfactory; but the fact that we have the means of making an early diagnosis in many cases, offers the hope that better treatment may be found.

VI.

HYDATID CYST OF THE LIVER.

By A. L. Mason, M.D., and H. L. Burrell, M.D.

The history of hydatid disease in this country is fortunately a very meagre one. About half a dozen instances have been found at the City Hospital in the past thirty years. Osler collected eighty-five cases from the United States and Canada, and a recent statistical paper by H. O. Sommer, United States Department of Agriculture,[1] states that only 100 cases including laboratory specimens are to be found in our medical literature, more than half the subjects being foreigners. While Echinococcus disease is not uncommon in England, it is from Australia that we derive our most recent knowledge of this affection which there causes a very large mortality as in Iceland.[2] In those countries the prevailing conditions favor its wide-spread distribution, viz.: General infection of dogs by the taenia Echinococcus and their close association with man and the ruminants (sheep, cattle, hogs). This small but prolific parasite is practically unknown in the United States, and there is seldom much ground for considering the presence of hydatid cysts in man.

In the differential diagnosis of hepatic enlargements, however, the following points should be borne in mind as suggestive of possible hydatid disease.

1. Previous residence in a country where that disease is prevalent.

2. A smooth, painless, elastic protuberance with bulging of the lower ribs.

3. Hydatid percussion fremitus, present in some cases.

[1] N. Y. Med. Journal, Nov. 23, 1895; Aug. 22, 1896.

[2] See Graham on Hydatid Disease.

4. Extreme latency of symptoms, often for years, as distinguished from abscess, cancer or cirrhosis.

An absolute diagnosis cannot be made without the discovery of hooklets, or of cyst membrane, in the evacuated fluid. Hydatid cyst may resemble a distended gall bladder and jaundice may occur with either. Spontaneous cure may follow the discharge of the cyst contents through any cavity that affords a free outlet, like the lung, stomach, bowel or bladder, but rupture into the pericardial, pleural or peritoneal sac is rapidily fatal unless surgical relief is at hand. Invasion of the lung or the pleural cavity through the diaphragm causes grave symptoms that can only be interpreted by finding bladders or hooklets in the expectorated fluid or in that which is withdrawn by tapping.

The case here recorded, which was successfully operated on by Dr. Burrell, was first tapped in the Medical Department. Pus, subsequently found to contain membrane from an echinococcus cyst, but no hooklets, was evacuated from the right lobe of the liver.

DR. BURRELL'S REPORT.

In the small experience that I have had with the hydatid cysts of the liver (which is confined to two cases) their presence was not known prior to operation.

In the first case, which occurred in 1887, an exploratory laparotomy was being done, for a supposed cyst of the kidney, when suddenly the characteristic cysts were evacuated from an enclosing capsule. It was found that these cysts came from just beneath the right lobe of the liver; there was no suppuration accompanying their presence, and the cavity wall was stitched to the parietal peritoneum and the patient recovered.

The second case is as follows: G. H., October 28, married, waiter. He entered the surgical service, Jan. 22, 1896. Patient lived in South America for four years, but he left there nine years ago — since then has lived in England, Canada and Boston. Ten years ago he had inflammation of the lung on the right side. From that time to the present date has been fairly well. About the 1st of November, 1895, after running hard, was taken with pain in the "pit of the

stomach." A day or two later he became jaundiced. When he went back to work he had pain over the liver and below the ribs, on the right side, and was not very strong. He worked two weeks after the attack of jaundice, but had so much pain over the liver and was so weak that he gave up his situation. Other symptoms were distress after eating, eructation of gas, water brash, and, of late, considerable dyspnoea, especially on exertion or on lying down. No vomiting. For four or five days before admission he had night sweats. No cough. Loss of weight. Bowels regular. Urine high colored and burning.

Heart. — No murmurs. Apex beat in mammary line.

Lungs. — Fair resonance over left chest and over right front, down to fourth rib, below which percussion is flat with absent breathing — diminished voice and absent tactile fremitus. Over right back there is fair breathing down to angle of scapula, below which signs are as in front. Noticeable bulging of lower chest wall on both sides.

Liver. — Upper limit at fourth rib. Lower limit one and one-half inches below costal border.

Abdomen somewhat distended, tender in right hypochondrium and flank.

January 21. Dr. Mason aspirated in the sixth space anterior axillary line and obtained thick yellowish green pus. Patient transferred to surgical service for operation.

Operation. — The patient requested operation. Etherized. A skin incision was made in the eighth right intercostal space in the axillary line, an aspirator needle was passed through the intervening tissues into what was supposed to be the right pleural cavity; a greenish pus-like fluid escaped. The incision was then carried down through the intercostal muscles to the pleura; the periosteum of the ninth rib was scraped back and an inch and a quarter of the rib was excised. An opening was then made into the pleura, but none of the greenish pus escaped. It was then deemed advisable to explore the liver, so a trocar was passed from the wound, through the diaphragm and into the liver. Three pints or more of the same greenish pus were evacuated, containing jelly-like cystic bodies. Two very large-sized rubber tubes (an inch and a half in diameter) were inserted into

Days of Month
20
21
22
23
24
25
26
M E
TEMPERATURE
PULSE BEATS
RESPIRATIONS
103°
102°
101°
100°
99°
98°
97°
NORMAL TEMPRE
TAPPED
OPERATION
120
110
100
90
80
70
60
50
45
40
35
30

the opening, traversing the *diaphragmatic sinus*, and extending three inches into the liver substance. A large sterile dressing was then applied. Came out of ether well.

January 25. — Passed a comfortable but sleepless night. Side dressed three times since operation. It is to be dressed every six hours. Temperature normal this morning. Dressings are stained somewhat yellow. On first dressing more of the cysts were found, and these cysts escaped intermittently for ten days.

January 29. — Temperature has continued practically normal. Patient seems very comfortable. Discharge decreasing. Tube irrigated out every six hours.

February 1. — Tube irrigated out every eight hours. Patient sitting up with bed rest. Having solid food. Does not complain of pain. Face seems fuller. More color.

February 4. — Discharge has diminished very much. Patient's general condition improving fast. Sitting up a few hours each day.

February 7. — Drainage tube removed; two small drainage tubes inserted, passing in about two and one-half inches. Dressing changed twice a day. Percussion seems to show a decrease in size of liver, especially of left lobe.

February 13. — Only one drainage tube in wound now, passing in about two inches. Dressing changed twice a day. Patient has been up in clothes for several days.

February 18. — Patient had an attack of nausea and vomiting, general malaise yesterday. To-day there was a large increase of discharge from the wound of a jelly-like material. Patient feels much better.

February 23. — Discharge much lessened. Tube out. Iodoform wick inserted for about two inches. No return of constitutiona symptoms.

February 29. — Sinus is gradually closing up. Still a slight discharge. Dressed daily. No further constitutional symptoms.

March 5. — Patient had another slight attack of pain in the right side, some nausea, no vomiting.

At this time there was found to be a considerable enlargement of apparently the left lobe of the liver. There was marked epigastric fullness, an increase in the area of flatness,

and it was a question whether there was not another hydatid cyst in the left lobe.

Dr. Mason saw the case in consultation and found compensatory enlargement of the left lobe.

The operative treatment of hydatid cysts may be divided as follows: A, aspiration; (1) simple (2) combined with medicated injections, as for example, iodine, corrosive sublimate, permanganate of potash. B, exposing of the cyst and stitching the wall of the cyst to the parietal layer of the peritoneum and opening the cyst after the peritoneal adhesions have formed. (Simons' method.) C, Direct incision of the cyst. (Lindemann's method.) D, Electrolysis.

These four different methods of operating it seems to me are applicable under varying conditions. Aspiration, or aspiration combined with the injection of astringent fluids or electrolysis would be rarely advisable. Aspiration at best would be simply temporizing and at times the aspirated fluid would not give positive evidence of the presence of the echinococcus cyst. Wherever there is pus there can be but little doubt but that a free exit should be given.

The steps of the operation by the method of direct incision may be briefly stated as follows:[1]

"When the cyst is situated in the abdomen, the most prominent part is selected, and an oblique incision, about two inches long, is carefully made down on to the surface of the peritoneum."

"All bleeding points are picked up and ligatured, and then the peritoneum, to a corresponding extent is opened."

"The assistant presses carefully on the abdominal wall so as to allow the exposed part of the cyst to come closely to the wound. Two large sponges are kept closely applied to the opening to readily absorb any fluid which may escape when the cyst is entered, and prevent its passing into the abdominal cavity. Then with a handled curved needle, armed with silk, four stitches are passed attaching the cyst to the edges of the abdominal incision. The cyst is then opened with the knife, and the finger immediately inserted. It is further secured by additional stitches, to ensure its complete and safe adaptation to the external wound. The con-

[1] Graham, "Hydatid Disease," p. 163.

tents are thoroughly evacuated, the daughter-cysts extricated when necessary by means of a pair of suitable forceps. Great care is taken to completely empty the cyst, as retained pieces of membrane readily suppurate. This is best ensured by irrigating the cavity with some mild antiseptic lotion, such as boro-glyceride or boric acid, until all the original contents are brought away with the return flow."

"The parent cyst-wall will, in many cases, be found to collapse as soon as the fluid contents are removed, when it can be easily caught hold of by the forceps and extracted. If it still remain in situ, gentle traction should be made with the view of separating it from the ectocyst, but anything like force must be carefully avoided, as the vessels in the connective tissue of the outer covering, in some cases are numerous, and might easily bleed if forcible separation were attempted."

"The operation is completed by inserting a large perforated rubber drainage tube and the wound dressed with firm pads of suitable material. The dressing will have to be changed frequently for the first twenty-four hours, as the discharge is usually considerable."

In connection with the aspiration of hydatids the observations of Boinet are of interest. Boinet[1] has isolated from hydatid cysts of the liver a ptomaine, three milligrammes of which injected under the skin of a mouse caused death in five minutes; five centigrammes injected into the veins of a rabbit produced convulsions, first accelerated, then retarded respiration, rapid action of the heart, dilatation of the pupils, and lowering of the temperature to 80° F. (26.7° C.). Death was preceded by a few convulsive attacks.

Boinet records the case of a patient who, after aspiration, succumbed with rapid respirations, convulsions and paresis of the lower extremities.

The puncture and electrolysis of hydatids apparently modifies the clear fluid into a yellowish, turbid, syrupy liquid, rich in albuminoid matters, and in this is found more abundantly the above toxine. It resembles the mytilotoxin of mussels. The still intact hydatid vesicles are apparently acted upon by these ptomaines, causing aseptic necrosis and death.

[1] Medical Record, New York, April 14, 1894.

The presence of these ptomaines which develop from the hydatids is a possible explanation of the fatality which occurs from the bursting of hydatid cysts into the general peritoneal cavity, so that unless some direct contra-indication exists it would be better to immediately evacuate any hydatid cyst.

The stitching of the cyst-wall to the parietal peritoneum and the formation of adhesions might be applicable under exceptional circumstances. The method is tedious, and subjects the patient to the shock of two operations. If the direct incision and immediate evacuation of the cyst can be carried out with great care, the danger of infection of the general peritoneal cavity will be slight.

It is of interest to note in the case of G. H. that the pus and the hydatids were thoroughly evacuated through the so-termed diaphragmatic sinus, and this was done without stitching the diaphragmatic layer of the pleura to the parietal layer. These were undoubtedly adhesions which walled off the pleural cavity, so that general infection of the pleural cavity did not take place. By freely excising the ninth rib and by placing two very large tubes in the abscess cavity in the liver, sufficiently free exit was afforded to the pus and the cyst.

The evacuation of a cyst of this description is very characteristic. First there comes a quantity of gelatinous material. Then roll out the cysts, varying in size from one to ten cm. in diameter. These cysts keep coming faster and faster until the whole cavity is evacuated.

In this individual case the quantity of pus was estimated to be three pints, and the amount of echinococcus cysts one pint, making in all two quarts. The odor was very offensive. The finger was introduced into the cavity in the liver in order to evacuate all of the cysts.

The important point in this operation was to afford perfectly free drainage, and no attempt was made to irrigate out the cavity as the patient's condition was so feeble that it was considered wiser to allow the pus to discharge freely into the sterile dressing, and to have this re-adjusted every few hours, if necessary.

The patient was actively stimulated with strychnia, atropia and brandy. Heat and stimulants were kept applied constantly until he recovered from the shock.

The pathological examination of the pus and of the cysts was as follows:

1. "Abscess of Liver. Membrane of Echinococcus Cyst. No hooklets found."

2. "Abscess of Liver. Echinococcus Cyst (two tubes). Pyogenic bacteria (?) Pneumococcus in pure culture. Rabbit inoculated." Wm. T. Councilman, M.D.

For a long time after the operation there was a discharge of yellowish fluid from the wound which was unquestionably bile, as was shown by the following examination which is appended: "Liver Abscess. Pieces of gauze dressing for bile (?) The gauze, with discharge, is found to contain considerable bile." J. B. Ogden, M.D.

The principal danger from hydatid cysts is the possibility of their bursting into the general peritoneal cavity in which case a fatal result is almost inevitable. In case this should occur the peritoneal cavity should be washed out with a sterile salt solution.

Hepatic surgery is becoming better established. Practitioners are *recognizing* more clearly the necessity for early interference in pathological lesions of the liver and its adjacent structures. Under these conditions hydatid cysts will undoubtedly be found oftener and many patients suffering from obscure hepatic diseases will be relieved.

VII.

SURGICAL ABSTRACT.

By Herbert L. Burrell, M.D., and John T. Bottomley, M.D.

The bare statement, that 1,646 operations were performed during the last year, taken from the Trustees' Report, scarcely conveys an adequate idea of the amount of work done in the Surgical Department.

From the large number of operations that have occurred, a few groups of cases have been selected on account of their marked interest. In a way they represent the classes of patients that are continually presenting themselves for treatment at the hospital, and, while these cases are perhaps not remarkable, they illustrate certain points in diagnosis and in treatment that may be of surgical interest.

That 1,646 operations were done during the year means that there was an average of four or five surgical operations done each day; naturally, some days were busier than others; for example, on Nov. 8, 1896, eleven regularly scheduled operations were done, and they included an appendectomy, a radical cure of femoral hernia, a lithotrity and an amputation of the foot; on May 10, eight operations were done, and among these were a laminectomy, a laparotomy for an abdominal tumor, another for salpingitis, and a nephrectomy; on September 13, there were eight operations, and the more important were a laparotomy for a pelvic tumor, two laparotomies for extra-uterine pregnancies, a resection of the intestine for rupture, a radical cure of inguinal hernia, an amputation of the breast and an external urethrotomy. During the month of March, 152, and during the month of August, 154, operations were done at the hospital.

As illustrating the quantity of work done on the surgical services of the hospital, it is interesting to note that during the year 436,500 yards of gauze were used. The item of expense for ether alone during this period was $2,000.

During the past year 3,555 patients were treated in the beds of the surgical services, and while the number of patients has increased there is also greater care given to individual patients. Although the new operating theatre is not yet completed, it is now possible to have seven operations going on at the same time, each operator being in a separate room.

At the end of this article will be found a table of the statistics of major amputations which have taken place in the hospital since Jan. 1, 1894. There is also a summary of the amputations done since 1880, and as a matter of comparison another table is appended which shows the amputations which were performed from the foundation of the hospital to 1880.

During the past eighteen years 369 major amputations were done, and during that period there were admitted 44,970 surgical patients. During the first sixteen years of the hospital 368 amputations were performed, and during that period there were admitted 17,815 surgical patients.

These figures show clearly the great conservatism that has come with the advent of antisepsis. For in the period from 1864 to 1880, 2.01 per cent. of the patients' limbs were amputated, and from 1880 to 1897 .821 per cent. of the patients' limbs were amputated. A still further improvement has occurred in the past five years in that .591 per cent. of limbs were amputated.

The comparison of the mortality of the amputations of the different periods is of interest. In the period between 1864 and 1880 there was a mortality of 33.7 per cent. From 1880 to 1897 there was a mortality of 17 03 per cent. In the period from 1894 to 1897 there was a still further diminished mortality of 11.84 per cent.

SELECTED CASES OF INTEREST FROM THE SURGICAL SERVICES FROM JAN. 1, 1894, TO NOV. 1, 1897.

ABDOMINAL CASES.

Abdominal Aneurysm. Operation. Death.

John A., aged forty-six, a native of Finland, a machinist, entered the service of Dr. Munro, April 7, 1897. He com-

plained of pain in the left lumbar region, which had gradually increased till it extended into the left inguinal region and down the back of the left thigh. This pain had been constant and severe. There had been no vomiting nor chills. Physical examination showed a ventral hernia, beginning at the anterior superior spine of the ilium and extending downward and inward parallel to and just above Poupart's ligament for about five inches. There was tenderness along the course of the left sciatic nerve. The superficial veins of the left lower extremity were enlarged. No venereal history.

The case was believed to be one of sciatica, and he was transferred to the medical service, where he obtained relief from pain. When he left the hospital on April 28, the left leg was not freely movable.

He re-entered the hospital, May 19, 1897, a very sick man. The chief subjective symptom was very severe pain in left loin and iliac region, extending down the back of the left thigh. The left loin and iliac region was occupied by a tender, pulsating mass, dull on percussion. In a few hours the patient grew worse and the dull area in the loin increased in size. The pulse became rapid.

A vertical incision through the abdominal wall was made, two inches inside the left anterior superior spine of the ilium, and there finally came into view a black intraperitoneal tumor which extended from the brim of the pelvis to the kidney, and from the aorta to the flank, without any pedicle or apparent origin.

The tumor was opened and much fresh blood clot escaped. This first cavity was found to connect by a small opening with a similar cavity, in the region of the kidney. The kidney seemed to merge below into a retroperitoneal mass of clots, and was itself evidently pushed upward and forward. It was supposed that the mass was a much enlarged, lobulated kidney, into which, posteriorly and inferiorly, a large hemorrhage had occurred. The cavity, however, was explored and found to open into the aorta. Much fresh blood escaped, the cavity was packed with iodoform gauze, and the wound partially closed. The patient died in twelve hours.

This case of dissecting abdominal aneurysm shows how carefully the possible causes of sciatica should be considered. Careful palpitation of the abdomen, when the patient was first in the hospital did not reveal any tumor, and yet in six weeks the abdominal aneurysm had increased in size so as to fill the whole left iliac region and be plainly visible.

Retro-Peritoneal Sarcoma. Operation. Death.

L. G. C., aged fifty, entered Dr. Gay's service on Aug. 13, 1896, for the relief of constipation and abdominal pain. He had been confined to bed or to a chair for nine months, during which time he had had almost constant pains in the back and the abdomen; the pain extended down the inside of his thighs, and was worse when he was lying down. Constipation was a marked symptom; even under the use of cathartics his bowels moved only once in two or three days; the stools had been tape-like in character. He had lost some weight. His chief complaint was very severe pain in his back.

He had been similarly ill for four or five months five years ago. At the end of that sickness he was well enough to go to work.

Physical examination showed a heart somewhat enlarged. The examination of the abdomen, except for an area of tenderness in the right inguinal region and dilatation of the veins of the abdominal wall on the right, revealed nothing. The patient looked cachectic.

A laparotomy was done by Dr. Munro. The intestines appeared normal. The pancreas presented close below the parietes and the coeliac axis, portal veins and vena cava inferior were very superficial; both the latter as well as the mesenteric veins were abnormally distended. The stomach was displaced downward. A solid tumor was felt more distinctly on the left, apparently lying across the aorta. An attempt was made to reach this retro-peritoneal mass, but a number of very large veins were torn and there was a brisk hemorrhage controllable only by pressure. The mass could not be differentiated from the kidneys, and a "horseshoe kidney" was considered probable. On account of the hemorrhage

it was necessary to end the operation without further exploration. Patient died of shock in forty-eight hours.

The autopsy showed a large retro-peritoneal sarcoma, originating probably from the lymph glands, and it extended from the arch of the aorta to its bifurcation, completely surrounding its entire length. The tumor was enlarged at its upper and lower portions and below it bulged out laterally to the kidneys, so that, though the kidneys were normally situated, they could not be differentiated from the mass except by dissection. The pancreas and vena cava rested on the mass. The stomach was much dilated.

Retro-Peritoneal Lipomata. Partial-Removal. Death. Autopsy.

Thomas K., aged 44, was admitted to the service of Dr. Burrell, Jan. 6, 1897. He had used alcohol excessively up to two years before. Antecedent history otherwise negative.

Eight months before the patient had found a bunch about as large as a hen's egg in the right iliac fossa. At that time he had had no symptoms which called attention to that region, and the discovery of the tumor was accidental. After he found it he had more or less pain in the right side of his abdomen, especially after eating. The tumor had increased in size. The patient had lost weight and strength. He was a fairly well-nourished man. His temperature was normal, and his pulse 70.

In the right side of the abdomen was a large tumor, most apparent in the right iliac fossa. It could not be differentiated from the liver dulness. It was hard to the touch, and irregular in shape. Air was forced into the colon per rectum, and the abdomen was tympanitic to the edge of the tumor, so that it seemed probable that the bowel ran behind the tumor.

A tumor of the abdominal wall, tumor of the omentum, and tumor of the liver were considered as possibilities.

Observation of the patient for a week brought out no new facts, and finally a laparotomy was done. The peritoneal cavity was opened, and a large yellowish tumor was discovered, still covered by the retro-peritoneum. This covering was incised, the mesentery was traversed, and the obvious

tumor was finally shelled out. The lipoma was retro-peritoneal in situation, and was about the size of a cocoanut. There was only slight hemorrhage. The abdominal wound was partially closed. Gauze drainage was established, as the mesenteric vessels had been injured and some three inches of the intestine had been possibly robbed of its circulation.

On the second day after the operation the patient began to vomit and his temperature and pulse rose rapidly. These symptoms continued, and on the fourth day general abdominal tenderness developed. Discharge from the wound contained faecal matter. The patient died one week after operation.

Autopsy showed general peritonitis. There were many ulcerations of the ascending colon, with gangrene of the gut. Mesenteric vessels were thrombosed. Lying behind the ascending colon was another lipoma, which extended up to and above the diaphragm and down to the pelvis; it occupied the whole of the posterior part of the right side of the abdomen and the mass extended well over to the left kidney, covering the whole of the abdominal aorta.

At the time of the operation this mass was so uniformly distributed that its presence was not suspected.

It was easily shelled out and weighed 2,400 grammes. Tumor removed at operation weighed 1,070 grammes.

* * * *

In the cases of abdominal aneurism and the retro-peritoneal sarcoma, pain in the back and thighs was a very prominent symptom, and in each case the pathological cause was very different. In all the cases it was very difficult to differentiate clearly the kidney from the surrounding mass, even when the abdominal cavity was open. They show clearly that we may have an abdominal mass of considerable size and yet not be able to gain much information from either an external examination or a laparotomy.

Three cases of intestinal obstruction due to adhesions or bands. Operation. Recovery.

Annie C., aged thirty-three, single, entered Dr. Munro's service, April 19, 1897. Five months before she had had a laparotomy for the removal of a cystic ovary. She felt prefectly well until six days before entrance when she was

seized with abdominal pain which centred about the umbilicus and was associated with nausea and vomiting. For forty-eight hours following this attack she had diarrhœa; and six days later when she entered the hospital her bowels had not moved for four days. The abdomen was distended and tympanitic — resistant to pressure everywhere, but nowhere tender. The temperature was 100°. Enemata, high and low, failed to relieve. Dr. Munro did a laparotomy. A tough adhesion band, one-sixteenth inch in thickness, was found passing from the convexity of the large intestine to the mesentery, constricting an entangled loop and practically occluding it. The band was tied off and cut. The entangled loop was a small intestine. The operation gave entire relief.

Mary W., aged twenty-three, entered Dr. Gay's service, Oct. 12, 1896. She had been ill three days with general abdominal pain, which was especially severe about the umbilicus and in the right iliac region. Patient had been vomiting a great deal since pain began and had had a marked chill the morning of her admission. There was a history of two much less severe attacks in the preceding month. All the attacks came on suddenly and at night. The patient looked sick. Her face was pinched, the tongue dry and coated. The abdomen was somewhat distended and generally tender, but especially so high up in the right inguinal region, where there was muscular spasm and rigidity just above the crest of the right ilium; this seemed "too high for an appendicitis."

A laparotomy was done by Dr. Munro and nothing abnormal was found except that toward the median line and passing from above downward for about four inches, lying in front of the iliac vessels, but not touching them, was a tense band of adhesions; adherent to, and probably constricted by, this band was a loop of small intestine that was much congested, and at one point showed a patch of lymph. The band was easily broken. It probably originated from some part of the mesentery of the small intestine. The cæcum was found in a somewhat higher position than usual, and the appendix pointed backward and upward and the tip was buried in old adhesions. It was very small, not inflamed, and was apparently quiescent. It was tied off and removed. Operation gave complete relief.

Annie B., aged twenty-six, patient of Dr. Post. On July 4, 1894, she was transferred from the Gynaecological Department for operation. She had had severe abdominal pain for three days, and obstinate constipation in spite of cathartics. She entered the surgical service in a state of collapse, and a laparotomy was immediately done by Dr. Post

On opening the peritoneal cavity considerable bloody serum escaped. The small intestine was found to be dilated to four times its normal size and to be of a purplish color. Two tough adhesions bands were found running, one from the top of the uterus and the other from the right fallopian tube to the small intestine and drawing the gut into a knuckle. These bands were ligated and cut. Immediately the small intestine began to regain its normal color and to collapse, while the large intestine began to inflate.

The patient was discharged from the hospital in four weeks, in excellent condition.

* * * *

These three cases illustrate one cause of intestinal obstruction. In the first case the obstruction was probably due to an adhesion following a laparatomy; in the two others the adhesions were due to some old inflammatory process in the peritoneal cavity. In cases of intestinal obstruction where there is a history of an operation or an attack of peritoneal inflammation the cause may be inferred. The greatest danger in intestinal obstruction is delay in operating. The symptoms in the beginning are generally rather mild, and for that reason operation is often deferred so long that when it is done the case is almost hopeless.

Volvulus. Intestinal resection. Death.

Edward F., aged 44, patient of Dr. Monks, entered the hospital on Nov. 13, 1894. A week before he "caught cold," and, though he had had headache and considerable abdominal pain, he had worked for four days. Meanwhile his bowels had not moved. On the fifth day his symptoms became much worse, and vomiting began, and continued till time of entrance. Cathartics had no effect upon the constipation. At entrance the patient was suffering intense pain in abdomen; he had a temperature of 103.4 degrees and a pulse of

120. His abdomen was considerably distended, everywhere tender; there was flatness on percussion, and some resistance in the right inguinal region. There was some dulness in the left inguinal region. The rectum was empty.

An immediate laparotomy was deemed necessary. On opening the peritoneum a large quantity of amber-colored, purulent fluid escaped. There was general peritonitis, — and a much distended portion of the large intestine, fifteen inches in circumference, presented. This was incised and the contents allowed to escape; the incision was closed, and the gut returned to the peritoneal cavity. The sigmoid flexure was found to be gangrenous, and twelve inches of the large intestine were excised, and the ends were united by a Murphy button. Patient survived but a few hours. Autopsy showed a volvulus of large intestine and sigmoid flexure. Cause of strangulation not ascertained. No thrombosis of the vessels.

Intestinal obstruction due to a tumor. Formation of artificial anus. Relief.

David B., aged 56, patient of Dr. Burrell, entered the hospital, Nov 29, 1895, for the relief of obstipation of a week's duration. The man had been perfectly well, as far as he knew, up to five weeks before; then he began to be constipated and this has continued and has finally culminated as above. He had had considerable abdominal pain which was not localized. His abdomen was very much distended, but was not tender. There was no history of vomiting. On examining by rectum the finger detected a tumor which at first seemed to occlude the passage. Careful search, however, revealed an opening. The tip of the mass felt like the cervix uteri, only the sides of the opening were roughened. Patient had a specific history.

The man was put on iodide of potassium and small daily doses of castor oil. His bowels moved daily for a few days, but the movements were small and the abdominal pain and distension were not relieved. His temperature remained about normal, but the pulse gradually increased in rate.

Operation was considered necessary and a colotomy was done through a three-inch incision, just inside the left anterior superior spine of the ilium and an artificial anus was formed.

The operation gave great relief to the patient and the abdominal distention disappeared.

He remained in the hospital about four weeks and then went out in excellent general condition. He had daily two to three well-formed movements through the artificial anus. He passed nothing by rectum. The tumor mass showed no change and was probably not syphilitic in nature.

* * * *

The case illustrates the possibility of giving great relief by the formation of an artificial anus in cases of growths low down in the pelvis. The subsequent history of the man is not known.

Intestinal obstruction. Cause unknown. Formation of artificial anus. Spontaneous closure of artificial anus. Complete recovery.

Tony R., an Italian, twenty-four years old, patient of Dr. Dwight, entered the hospital, Nov. 17, 1896, with what appeared to be a typical attack of acute appendicitis. His illness was of six days' duration. He had pain pretty well localized in right iliac region, constipation and vomiting. His abdomen was somewhat distended and tympanitic. No tumor could be felt. He had some muscular rigidity on both sides of the abdomen, but his tenderness extended from the right inguinal region up into the lumbar region.

An immediate laparotomy was done, a three-inch incision being made over the region of the appendix. This organ was found to be perfectly normal and showed no evidence of inflammation. The peritoneum was injected and thickened. There was considerable plastic exudation and there were numerous adhesions between the coils of intestine. In the right pelvis was a loop of small intestine which was, or had been, strangulated. It was dusky and mottled, though it had not entirely lost its gloss. No cause of the strangulation could be found. The formation of an artificial anus was deemed the safest procedure, and it was accordingly done.

The operation was followed by a disappearance of the symptoms. There was a natural movement of the bowels the day after the operation. On the thirteenth day the patient's

temperature rose, but fell again after the opening of a superficial abscess at the seat of the artificial anus.

On the eighteenth day it was decided to operate again, because for some days there had been abdominal distension, abdominal pain, and patient was uncomfortable and restless. The abdomen was opened and the whole peritoneal cavity, except the upper third on the right side, seemed to be filled with pus. Peritoneal cavity was thoroughly washed out and drainage was established. The patient was completely relieved. Faecal discharge continued till the forty-ninth day, when it ceased entirely. The patient was discharged in three months perfectly well.

Two cases of perforation of the intestine by a typhoid ulcer. Laparotomy. Recovery in one case; death in the other.

Wm. J., an adult, patient of Dr. Munro, entered, Oct. 30, 1895. He gave a history of about two weeks' illness, the chief symptoms of which were malaise and marked diarrhœa. A diagnosis of typhoid fever had been made by his attending physician. Three days before entrance he was very suddenly seized with a sharp, severe pain in the right iliac region; intense nausea and vomiting followed almost immediately. The pain in the abdomen became more or less general, but was particularly well marked in the right iliac region; these symptoms, with constipation, continued till he entered the hospital.

The patient was very sick and looked typhoidal. His abdomen was distended, tympanitic and generally tender. There was comparative dulness and marked muscular rigidity on the right side below the umbilicus. The spleen was enlarged and the abdominal wall showed doubtful rose spots. No tumor could be felt. An immediate laparotomy was done by Dr. John C. Munro. An incision was made about half way between the umbilicus and the right anterior superior spine, and a well walled-off intraperitoneal cavity was opened about the size of a fist and filled with pus. The patient's condition at this time became so critical that search for the perforation could not be made, and the operation was completed by establishing drainage. The patient failed to rally and died in ten hours.

Permission for a complete autopsy could not be obtained, but an examination through the wound established the fact that the appendix was normal.

W. S., adult, patient of Dr. Watson, was transferred from the medical side on Sept. 29, 1825, with a history of eight weeks' illness from typhoid fever and recent symptoms indicative of perforation. The man's temperature was 102.5; his pulse 120; the abdomen was moderately distended and tympanitic. There was localized pain and tenderness rather high up in the right iliac region. An incision was made over this point. No pus was found in the peritoneal cavity. A loop of gut was found adherent to the parietal peritoneum and around this were strings and flakes of organized lymph. A perforation, about the size of a dime, of the small intestine, was found with some faecal matter escaping. Perforation closed with Lembert suture. The stitches had to be introduced so far back from the edges of the ulcer, that the lumen of the intestine was considerably diminished. The peritoneal cavity was washed out and the abdominal wound closed. The patient was discharged well in three weeks.

TWO CASES OF RESECTION OF THE BOWEL.

Tubercular disease of the caecum and appendix. — Resection. Recovery.

Frances F., aged twenty, patient of Dr. Burrell, entered the hospital, April 14, 1897, with the following history: Three weeks before entrance she began to have general abdominal pain which after a week became localized in the right inguinal region. Pain was sharp and intermittent. Patient had had a rather constant diarrhoea during this time. There had been no nausea nor vomiting. She had had two previous similar attacks. The family history was negative. Physical examination disclosed nothing abnormal in the heart and lungs. There was well localized tenderness in the right inguinal region, but no tumor was felt, nor was there any muscular rigidity.

A laparotomy was done and on opening the peritoneal cavity a necrotic condition of the caecum and appendix was found; the intestines in that region were matted together.

Seven inches of the colon (with the caecum and the appendix) and two inches of the ileum were resected.

The ends of the intestine were joined together by two layers of Cushing's right-angle continuous suture. The first layer took seven and a half minutes to complete, and the second layer four minutes. A small wick led down to the sutured intestine for drainage. The whole operation occupied thirty-seven minutes. The patient's convalescence was without notable incident. There was no return of the symptoms, and the patient went out in five weeks in excellent condition, having gained considerable weight. She was seen seven months later and was perfectly well.

Criminal abortion. Ignorant resection of intestine. Laparotomy. Operation resections. Peritonitis. Death.

Loretta S., twenty-six years of age, patient of Dr. Munro, had a criminal abortion two days before her entrance to the hospital, April 23, 1897. Within thirty-six hours after the abortion she was seen by the abortionist, who, not finding the patient as well as she expected, summoned a friend in consultation. The friend found a black mass protruding from the vulva and cut it off. This, upon examination, proved to be intestine, and a physician was called in, who immediately sent the patient to the hospital. Upon entrance the patient did not look ill. The abdomen was soft, not distended, and was slightly tender in the lower third. Hanging from the vagina was a piece of black, gangrenous gut, about seven inches in length, from which there was very slight hemorrhage. Laparotomy was done immediately. A ragged rent, one inch long, was found in the top of the uterus, which gave passage to and constricted a loop of intestine. The constricted gut was black and gangrenous for some distance from the constriction. Sixteen inches of the small intestine were resected, the hemorrhage from the mesentery being controlled by a button-hole suture. The cut ends of the gut were brought together by two layers of Cushing's right-angle continuous suture. The rent in the uterus was closed by a mattress suture. The uterus was curetted out and irrigated. The peritoneal cavity was

washed out with several gallons of sterile water, and the pelvis was drained through the abdominal wound.

The patient died in eighteen hours of peritonitis.

FOREIGN BODIES IN THE DIGESTIVE TRACT.

Mary W., aged twenty-four, patient of Dr. Gavin, was admitted to the hospital, May 17, 1896. She complained of mild epigastric pain, which she had felt since early in the afternoon, when, while eating, she had swallowed three artificial teeth attached to a plate. The family administered large quantities of mustard and water, with no effect other than to cause active emesis. A careful examination failed to give any further information, and the patient was put to bed. Two days later the teeth and plate were passed in the stools.

Cornelius C., fifty years of age, patient of Dr. Munro, entered the hospital, June 29, 1896, complaining of pain in left side of abdomen; the pain was of sudden origin and accompanied by a chill; it had been constant and was especially severe when he coughed. His bowels were constipated. The whole upper left flank was indurated and brawny. The overlying skin was red and the whole area was tender.

The patient was in the hospital a week before he would consent to an operation. During that time he suffered much pain, and the induration had spread to the front of the abdominal wall.

An incision was made along posterior edge of the external oblique, and after breaking through much necrotic tissue there was discovered, between the peritoneum and abdominal wall, a large trabeculated cavity from which there escaped a quantity of very foul pus. The cavity ran upwards beneath the ribs and in its upper part was found a foreign body which proved to be a fish bone.

The abscess cavity granulated in slowly. Patient had no further symptoms.

Burton F., twenty-seven years of age, patient of Dr. Bradford, entered the hospital, Feb. 14, 1894, with the following history: Two hours before entrance during a fit of sneezing he had swallowed two artificial teeth and the

attached plate. Free emesis was artificially produced but without bringing up the lost teeth. He thought he could tell just where the foreign body was and put his finger on the hyoid bone. Pressure there caused pain. A bristle probang passed into the stomach without difficulty and without result. Patient was put to bed, and in five days, at his own request, was sent home, his only symptom having been "sore throat."

Five days after his discharge he returned. He had spent the whole five days in bed, and returned because of two or three sharp hemorrhages. The blood which was expectorated was fresh in appearance and apparently came from the pharynx. He had had no vomiting. Physical examination was absolutely negative, except that patient was rather blanched by the hemorrhages. Oesophagotomy was performed by Dr. Bradford, under chloroform. An incision three inches long was made along anterior border of sterno-mastoid muscle on the left side. On opening the oesophagus the rim of the plate was immediately felt; the plate was lying with its convexity fitting into the concavity of the dilated oesophagus, with its long diameter up and down, thus explaining why sounds and bougies had slipped by without revealing the presence of a foreign body. No pus was found. Oesophagus closed by silk sutures.

He took some milk by mouth in twenty-four hours, though feeding was principally by nutrient enemata. Feeding by mouth was gradually increased and enemata were omitted after the sixth day. No leakage of fluid from wound after two weeks. Discharged well three weeks after operation.

* * * *

These cases are very interesting as showing the possible behavior of a foreign body in the digestive tract. It may be passed per rectum as in Case I. It may ulcerate through some point in the digestive tract causing the formation of an abscess, as in Case II., or cause serious hemorrhage, as in Case III.

The hemorrhage may be a very serious one, because of the relation of the œsophagus to the aorta and to the azygos veins. Emesis may result in bringing up a foreign body,

even after it has been lodged in the digestive tract for some time. Dr. G. W. Gay, in the third series of City Hospital reports, cites a case of a leaden quarter of a dollar being thus removed five and a half months after its being swallowed.

A point well illustrated in Case III. is that there may be a foreign body in the œsophagus and still it may not be dislodged or even detected by a probang or bougie.

ABSCESSES OF THE LIVER.

James Q., aged sixty-four, a tailor, patient of Dr. Gay, entered the hospital, July 28, 1897, with a large, tense, hard mass, feeling like an enlarged or depressed liver, in the epigastric region, and extending into the right hypochondrium. The mass was markedly tender. There was slight, but general, abdominal distension. The patient looked sick, had a sub-normal temperature and a pulse of about 80.

The patient was attacked suddenly eight days before entrance with pain in the epigastric region. For five days his bowels did not move; in the following three days they moved moderately. He had kept up and about, but was very weak and had been vomiting some. No history of dysentery could be obtained. The patient had had several attacks, similar to the present one in the last four years.

There was a friction rub over the right base in front, and a sub-phrenic abscess was considered probable. On the day following his coming to the hospital the patient failed perceptibly, and died the next day.

The autopsy showed abscesses of the liver which were amœbic and were secondary to a number of ulcers in the carcum. There were four abscesses in the liver and the pus was yellowish gray; there was 200-300 cc. of pus in the peritoneal cavity.

Cornelius W., patient of Dr. Munro, entered the hospital, Aug. 11, 1896, suffering from his third acute attack of appendicitis within six months. Immediate operation was done, and a thick, indurated appendix removed from a mass of adhesions. Drainage was used. The patient did very well for two weeks, and then developed a rising temperature which became intermittent, and the patient had many chills which

came at no definite time, but were irregular. Vomiting and diarrhœa were also present. Examination of the blood was negative, as was examination of the urine. Patient complained of some pain along the right costal border. No enlargement of liver was detected. The pain under the right costal border became so severe that an exploratory incision was made on September 13, and nothing was found except a bulging of the right lobe of the liver. A trocar was inserted into this, and also into the right pleural cavity without result. The operation had no effect on the patient, and the irregular chills, the vomiting and the diarrhœa continued. One week after the operation the edges of the wound, beneath costal border, separated spontaneously, and a large quantity of bile-stained pus escaped. His symptoms were not relieved, however, but a cough and very profuse foul expectoration began. All these symptoms (except the diarrhœa, which ceased the first week in October) continued until the first week in November, the discharge from the liver abscess being especially profuse and foul. After the first week in November, however, the discharge gradually grew less and the patient continued to improve, and left the hospital on December 7, feeling perfectly well.

The patient was so ill that it seemed actually impossible for him to live. His chills were very severe and very depressing. He could take no food at times by mouth, and he became extremely emaciated. He was fed by rectum for a long time. When he was able to take food by mouth he was given it very often, but in small quantities. This was continued day and night; he took large quantities of milk in this way, and to the nourishment and heavy stimulation his recovery is due.

HEAD CASES.

Exostosis of bones of face and skull. Multiple operations. Death.

Frank W., aged thirty, patient of Dr. Burrell, entered the hospital, April 6, 1897, for the removal of an exostosis of the right temporal bone. His previous history is interesting and worthy of notice.

Feb. 11, 1886, he was on Dr. Cheever's service in this hospital for bony growths of the bones of face. The two

largest tumors were situated one on either side of his nose just below the eyes; the one on the right side was as large as a small hen's egg, that on the left as an English walnut. There was a similar nodule on the left zygoma and one on the right inferior maxilla. At that time he had difficulty in breathing; the arch of his palate was very high and narrow, and his eyes were protruding. The bony masses on either side of his nose were chiselled off by Dr. Cheever.

June 13, 1888, he had a lachrymal abscess, which was opened and drained.

Feb. 9, 1889, he came for the removal of the process on the inferior maxilla. This had increased in size. Dr. Cheever removed that, and at the same time chiselled a piece off the right inferior maxilla, that it might correspond more nearly with the left. General condition was very good.

Nov. 4, 1893, he came because he had had for a year great difficulty in breathing through his nose and was deaf. By means of a trephine and burr-drill, a hole was made through solid bone from the posterior nares into the naso-pharynx. This afforded him great relief, the right nostril being well cleared.

His last appearance at the hospital (April 6, 1897) was for the relief of severe pain in and beneath the right eye and of difficulty in breathing through his nose. Both eyes protruded, the right more than the left; there was apparently more than the normal distance between the eyes; they seemed to be forced outward. In the right temporal region was a hard, round mass, protruding about one-half an inch and about two inches in diameter, and somewhat tender. The head was very long up and down, and apparently very high above the ears. He could breathe through both nostrils. His voice sounded strange and muffled.

The prominence of the right eye-ball increased. There was distinct tri-facial neuralgia, and the tumor in the temporal region became tender and painful; for these reasons an operation was performed by Dr. Burrell, about a week after the patient entered the hospital.

A flap was turned back, and the periosteum was elevated from the surface of the tumor, which was found to be com-

posed of thickened and mammillated bone. An inch trephine opening was made just above the temporal ridge at the point of junction of the external angular process of the frontal bone and two and a half inches from the root of the zygoma as it springs from the temporal bone. A button of bone half an inch in thickness was removed. A triangular mass of skull with the tumor was then excised; the part removed extended from the root of the zygoma out to a little above the external angular process of the frontal bone. In accomplishing this the circular saw, the bone forceps, the trephine and the chisel were used; the dura was not injured.

Difficulty was found in separating the triangular piece from the external angular process of the frontal bone and a bit of the orbital process — part of the wall of the orbit — and some of the greater wing of the sphenoid were removed with it. The eye-ball could be seen through the opening into the cranial cavity. A large mass of osseous substance rested in the anterior fossa of the skull and seemed to extend back indefinitely, surely to the lesser wing and body of the sphenoid. As this could not be removed with safety, nothing further was done, and the wound was closed.

The operation did not relieve the patient; his eye-ball continued to project and finally enucleation was done. The orbit felt normal. The pain in the head continued, and the patient had several attacks of heart failure, and finally, on May 15, about a month after operation he died in one of these attacks.

The autopsy was unsatisfactory, inasmuch as permission could not be obtained to remove the skull in toto. The bones of the face and skull were everywhere thickened. The antrum was obliterated by the formation of new bone. The upper and middle turbinates could not be differentiated. The upper nares were entirely occluded, except anteriorly, where there was a passage along the vomer to the ethmoid. There was an abscess beneath the pituitary body and the tissue of the pituitary body had been destroyed and in its place was what was probably scar tissue.

The fact that there was a lesion of the pituitary body may, perhaps, partially explain the double exophthalmos and the ptosis.

Glioma of the brain. Sudden death.

James J., aged thirty-four, patient of Dr. Cushing, entered the hospital, Jan. 22, 1895, on account of an injury to his arm caused by his falling out of bed; the patient was said to have consumed five pints of whiskey before retiring; otherwise he seemed perfectly well. The arm was not broken.

At 2 A.M., January 25, he vomited once, without apparent cause. He said he then felt all right. He was seen at 5.30 A.M. by an orderly and seemed to be in good condition. At 6 A.M., when next seen, he had lost all power of motion in both arms and legs. There was nothing noticeable about the face; there was neither aphasia nor anaesthesia. The reflexes were absent. Respiration was carried on by the intercostals and diaphragm. Rales were heard over the whole chest.

At 4 P.M. he was in the same condition, and was apparently not suffering. He died very suddenly at 5.55 P.M.

The autopsy showed nothing worthy of note except in the brain. There in the lenticular nucleus on the right side was an area of the size of a chestnut into which there had evidently been a hemorrhage at some previous time. The tissue in this area was broken down, black in color and contained some calcareous material. It was apparently a new growth which had degenerated. The area projected somewhat into the lateral ventricle, but had apparently not ruptured into it. The growth involved the internal capsule. Nothing further was found in the brain, cord or brachial plexus.

Marquezy, in 1888, reported to the Anatomical Society of Paris[1] a case analogous to this. A man went to bed one night drunk and the next morning was found comatose with right hemiplegia. At the autopsy a tumor with a greenish caseous centre surrounded by a fleshy congested part was found. The tumor lay in the nucleus lenticularis and had invaded the internal capsule in its knee and posterior part. Pathologically, the tumor was sarcomatous.

The extraordinary fact in both these cases was the sudden appearance of the symptoms. In neither case did the patient have any symptoms of brain tumor till the fatal attack came

[1] Bull. de l'Societe Anat.

on. Whether the ingestion of large quantities of alcohol at one time had aught to do with hastening the process is a question.

Tubercular meningitis. Operation. Death.

Maud W., two and one-half years old, patient of Dr. Burrell, was brought to the hospital, March 16, 1896, in a semi-conscious condition; the mouth was open, the eyes open and staring. The right pupil was widely dilated and gave no light reflex; the left pupil reacted to light. Right side of face and head seemed to be hypersensitive. No tache cerebral. A diagnosis of tubercular meningitis with effusion into the ventricles was made. No history could be obtained with regard to the child or her condition. Small double trephine openings were made over the parietal eminences. Attempts were made to tap the ventricles, but no fluid was evacuated. The child had clonic convulsions and died in four hours. Autopsy showed acute general miliary tuberculosis with scattered tuberceles in the brain and pia and a tubercular thrombus of the longitudinal sinus.

THREE CASES OF ANTHRAX.

A wool sorter, twenty-seven years of age, patient of Dr. Post, entered the hospital, June 3, 1897, with a small, dark-brown area about one-half by three-quarters inch on the right side of the neck, near the apex of the submaxillary triangle. This area was surrounded by a row of small, clear vesicles and the tissues for the distance of an inch all around it were indurated. Four days previous to entrance, while feeling perfectly well, he had noticed a "small, red pimple" on his neck. The following day his throat was sore; two days before entrance, headache and malaise were first noticed, and his symptons gradually increased in intensity after that time. At the time of entrance he looked very sick, was restless, and had a temperature of 102°. Bacillus anthracis was demonstrated in lesion by a cover slip. The indurated area was excised, the parts thoroughly cleansed and the wound sewed up. The next day his temperature fell to normal and he had no symptoms or discomfort. Wound healed by first intention, and patient went home in a week.

Peter W., a freight-handler, aged twenty-six, entered the hospital, Jan. 6, 1895, as a patient of Dr. Cushing; he had been handling dressed leather and, at times, tanned hides, though he had touched none of the latter for two weeks before entrance. Four days before entrance he had noticed a "blister" on the right side of his neck. He felt all right until the day before entrance, when his neck became tender and painful and he "felt sick all over." He exhibited a typical lesion on the right side of his neck, three inches below his ear. About it was an indurated area and a hard, tender line could be traced downward and forward nearly to the sternum. The patient did not look very ill. His temperature was 101.8°, and his pulse 100. The bacillus anthracis was demonstrated.

The lesion and indurated tissue about it were excised, and a dissection was made by turning back the skin from the front of the right side of neck; the infected tissues which were black and sloughing were removed. The area was then thoroughly curetted and cleansed, packed with iodoform gauze, and the skin flaps brought together.

The patient made a recovery which was uninterrupted and without incident.

Daniel H., aged forty, patient of Dr. Post, a laborer in a leather store, entered the hospital, June 23, 1897, with the following history: Four days before, while shaving, he noticed a "pimple" on his neck. He pricked it with a needle, but gave no particular attention to it because he felt perfectly well. The next day he felt rather tired and stupid, but he worked all day. The following day brought no change, though, his wife said, he twitched a great deal as he slept; the twitching was confined to the hands and to the muscles of the neck. The day of entrance he felt sick — was nauseated and vomited and experienced a choking sensation.

On the right side of the neck, external to the line of the angle of the jaw and midway between that and the clavicle, was a lesion, oval in general form, about the size of a five-cent piece or smaller — moderately raised. In the middle was an eschar, about as large as the nail of the little finger. About the margin, at irregular intervals, were small vesicles. General induration of right side of neck. No enlarged glands.

The general condition was one of stupor, but he was rather easily aroused. Soon after entrance the patient had a marked epileptiform convulsion beginning in the hands and becoming general. Involuntary dejections. Convulsion lasted about fifteen minutes.

The lesion was excised. The patient failed in spite of heavy stimulation. He had another convulsion at 4 P.M., and died in a few hours.

No anthrax bacillus was found in swabs from the floor of place where patient worked or from the hides.

THREE CASES OF ACTINOMYCOSIS.

Sarah S., forty-eight years of age, patient of Dr. Monks, entered the hospital, Aug. 5, 1897, with a very much swollen left breast. The skin over the breast was not red, but very tense and glistening; the breast was fluctuant and very tender. There were numerous old cicatrices and sinuses on the chest wall below the cardiac area and in the scapular region, the result, she said, of multiple abcesses of those regions about seven years before her present illness. Some of these sinuses had been discharging ever since.

Nine years before her present trouble she had been operated on for left-sided "pleurisy." At the time of entrance the whole left chest was dull to percussion. The swelling of the breast began three weeks ago, when she discovered a small lump, which was tender and painful, a little above and outside the nipple. The breast has increased in size. The patient has had numerous chills, considerable cough and profuse expectoration.

Two days after entrance Dr. Thorndike incised the breast, and a large amount of pus was evacuated. It was very foul and showed numerous black specks. Immediately beneath the nipple was a hole which opened between the ribs into the pleural cavity.

The patient was greatly improved by the operation, and for five days progressed satisfactorily. She then suddenly collapsed, became hoarse and cyanotic, and died in twelve hours.

At the autopsy the following conditions were found: Two centimeters to the left of the lower end of the sternum, four

centimeters to the left of the nipple, and four centimeters below the nipple were the openings of sinuses that led down between the muscles and ribs into the pleural cavity or lung. From these sinuses came a thin, apparently purulent fluid, in which minute yellow specks could be seen, which specks on examination proved to be actinomyces. The left pleural cavity was obliterated. The left lung was airless and completely solid. In the centre were several large, rounded cavities, about the size of a hazel-nut and reddish in color. In other portions of the lung were several small foci, containing purulent looking material in which actinomyces were found. Tubercle bacilli were searched for but not found.

Hannah R., aged fifty-four, patient of Dr. Post, came to the hospital, June 18, 1896. Her left cheek was bluish in color, indurated, and from several sinuses there exuded a thin, purulent discharge. Three months before entrance her cheek had suddenly become sore and swollen. It was supposed that this was the result of decayed teeth. The swelling continued, and resulted in abscess formation. The abscesses opened externally, the first and most painful one just over the malar prominence. Bare bone could be felt through the sinuses; there was no glandular enlargement. There were carious teeth in the left superior maxilla.

Cultures from the discharge were negative. The sinuses were laid open and curetted out. The material was sent to the pathologist, who returned the diagnosis of actinomycosis. The operation failed to stop the progress of the disease, and an abscess appeared on the tenth day, back of the left ear. At the end of a month there were signs of the disease burrowing beneath the left sterno-mastoid, but the patient declined further operation and went home unrelieved.

E. C., male, aged thirty-four, patient of Dr. Monks, entered the hospital, Aug. 23, 1894. He was very sick and, being able to speak no English, objective symptoms alone could be obtained. He was breathing rapidly and laboriously, forty times to a minute. His temperature was 100.5°, and his pulse 102. The patient was very much emaciated, and over both lungs could be heard bronchial breathing and moist rales.

About one and one-half inches below the ensiform cartilage and running parallel with the costal border was a discharging

surface about two inches long, from which came a foul-smelling, whitish, purulent fluid. Between the tenth and eleventh ribs, about three inches to the outside of the wound mentioned above, was a small discharging abscess cavity. On both forearms, about three inches above the wrists, over the pronator muscles, and on the left shoulder, were tumors about as large as a hen's egg, fluctuant and evidently containing pus.

The patient was in a desperate condition, and lived only three days. He had a persistent diarrhœa (ten to twelve movements a day), and was a picture of general sepsis.

The autopsy showed a general infection with actinomycosis. There was a broncho-pneumonia, with secondary abscesses of the lung, peri-hepatic abscess, abscess of the kidney, abscess of the brain, hyperplasia of the lymphatic glands and acute splenic tumor. The sinuses in the chest wall ran beneath the ribs; and the sinus of the abdominal wall ran down to the peritoneum.

STATISTICS OF MAJOR AMPUTATIONS, FROM JANUARY 1, 1894, TO NOVEMBER 1, 1897.

By J. T. Bottomley, M.D.

Amputations at the Shoulder Joint. (Traumatic, Secondary.)

No.	Sex.	Age.	Nature of Injury.	Duration.	Methods.	Place.	Result.	Remarks.
1	M.	12	Necrosis of humerus	7 months.	Flap.	.....	Recovery in 3½ mos.	Very slight sloughing. Vide amp. of the arm. (Traumatic, secondary) No. 1.

Amputations of the Arm. (Traumatic, Primary)

1	M.	5	Crush of arm.....	Recent.	Flap.	Upper third.	Recovery in 5 wks.	Very slight sloughing.
2	M.	33	Traumatic amputation of arm.....	Recent.	Flap.	Middle.	Recovery in 3 wks.	
3	M.	11	Compound fracture of humerus...	Recent.	Flap.	Upper third.	Recovery in 3½ mos.	Multiple injuries, including compound fracture of leg.

Amputations of the Arm. (Traumatic, Secondary.)

1	M.	12	Compound fracture of both bones of forearm	3 days.	Flap.	Upper third.	Recovery in 6 wks.	Vide amp. at shoulder joint. (Traumatic,) secondary) No. 1.
2	M.	3½	Compound fracture of humerus...	5 days.	Flap.	Upper third.	Recovery in 9 wks.	Attempt to save arm. Beginning gangrene.

Amputations of the Arm. (Pathological.)

No.	Sex.	Age.	Nature of Injury.	Duration.	Method.	Place.	Result.	Remarks.
1	M.	66	Epithelioma of arm	2 years.	Circular.	Middle.	Recovery in 2 wks.	Recurred in axilla in two months.
2	F.	69	Fibro sarcoma of humerus.	3½ months	Flap.	Upper third.	Recovery in 10 dys.	

Amputations of the Forearm. (Traumatic, Primary.)

1	M.	17	Crush of hand	Recent.	Flap.	Lower third.	Recovery in 3 wks.	
2 ...	M.	38	Shattered hand. (Dynamite.)....	Recent.	Flap.	Upper third.	Recovery in 5 wks.	Other hand badly lacerated.
3	M.	36	Comminuted fracture of radius, compound dislocation of carpus.	Recent.	Flap.	Lower third.	Recovery in 2 wks	Multiple injuries.
4	M.	26	Shattered arm	Recent.	Flap.	Upper third.	Recovery in 4 wks.	

Amputations of the Forearm. (Traumatic, Secondary.)

1	M.	60	Painful stump. (Hand.).....	5½ months.	Flap.	Lower third.	Recovery in 5 wks.	Slight sloughing.
2	M.	31	Compound fracture of forearm....	3 weeks.	Flap.	Middle.	Recovery in 1 wk.	Fracture not treated in hospital.
3	M.	52	Cellulitis of hand.....	8 weeks.	Flap.	Middle.	Recovery in 10 dys.	Necrosis of radius and ulna.

Amputations of the Forearm. (Pathological.)

1	F.	22	Tuberculosis of wrist.....	4 years.	Flap.	Lower third.	Recovery in 6 wks.	

Amputations at Hip-Joint. (Pathological.)

1.....	M.	58	Osteo-sarcoma of thigh..... ...	4 months.	Wyeth's.	.....	Death, 10 weeks.	Exhaustion.

Amputations of the Thigh. (Traumatic, Primary.)

1.....	M.	19	Crushed leg	Recent.	Flap.	Lower third.	Death in 10 hours.	Picked up on R. R. track after lying there hours unnoticed. Death from shock and hemorrhage.
2.....	M.	16	Compound fracture of tibia and fibula.....	Recent.	Flap.	Lower third.	Recovery in 3 mos.	Fracture of other leg, too.
3.....	M.	adult	Compound comminuted fracture of femur	Recent.	Flap.	Middle.	Death in 9 hours.	Shock. Brought to hospital, twenty-four hours after accident.
4.....	M.	9	Compound fracture of tibia and fibula	Recent.	Flap.	Lower third.	Recovery in 5 wks.	Necrosis. One inch more of bone removed, three weeks later.

Amputations of the Thigh. (Traumatic, Secondary.)

1.....	F.	60	Traumatic gangrene of leg.....	6 months.	Circular.	Middle.	Death in 4 days.	Exhaustion.
2.....	F.	54	Ununited fracture of femur.....	5 months.	Flap.	Middle.	Recovery in 3 mos.	Some suppuration. Original injury had caused a slough, not healed at time of operation.
3.....	M.	34	Traumatic gangrene of foot. (Foot amputated)	2½ months.	Flap.	Lower third.	Relieved in 3 mos.	Atheromatous arteries. Secondary hemorrhage. Sloughing of flaps. Vide next case.
4.....	M.	34	Necrosis of femur.....	5 months.	Flap.	Middle.	Relieved in 2½ mos.	Secondary hemorrhage. Sloughing. Vide preceding case.

Amputations of the Thigh. (Pathological.)

No.	Sex.	Age.	Nature of Injury.	Duration.	Methods.	Place.	Result.	REMARKS.
1.....	M.	61	Diabetic gangrene of toe.....	2 weeks.	Flap.	Lower third.	Death in 48 hours.	Shock.
2.....	M.	26	Tubercular knee.....	5 years.	Flap.	Middle.	Recovery in 5 wks.	Discharging sinuses for years before operation.
3.....	M.	23	Contractions of spastic paralysis..	21 years.	Flap.	Lower third.	Recovery in 5 wks.	Slight sloughing.
4.....	M.	59	Tubercular knee.....	6 years.	Flap.	Lower third.	Recovery in 6 wks.	Discharging sinuses before operation.
5.....	M.	40	Gangrene of foot.....	6 weeks.	Flap.	Upper third.	Recovery in 2½ wks.	
6.....	M.	29	Anchylosis of knee.....	20 years.	Flap.	Lower third.	Recovery in 4 wks.	Slight sloughing of flaps.
7.....	M.	21	Sarcoma of leg.....	6 years.	Flap.	Lower third.	Recovery in 3½ wks.	
8.....	F.	40	Osteo-sarcoma of femur.....	3 months.	Flap.	Lower third.	Recovery in 3½ wks.	Slight sloughing.
9.....	M.	14	Acute osteo-myelitis of femur.....	7 weeks.	Flap.	Upper third.	Relieved in 3 mos.	Very large amount of pus. Pus in forearm also. Sinus open, when patient went out.
10.....	F.	29	Sarcoma of popliteal space.....	1 year.	.....	Middle.	Recovery in 3 wks.	
11.....	M.	63	Gangrene of foot.....	8 days.	Flap.	Lower third.	Recovery in 2 wks.	Thrombosis of popliteal artery.
12.....	F.	32	Osteo-myelitis of tibia.....	17 years.	Flap.	Lower third.	Recovery in 2 mos.	
13.....	M.	33	Thrombosis of popliteal vessels..	5 weeks.	Flap.	Lower third.	Recovery in 15 wks.	Sloughing of flaps.
14.....	M.	79	Gangrene of leg.....	4 weeks.	Flap.	Lower third.	Death in 3 days.	Exhaustion.
15.....	M.	68	Gangrene of foot.....	3 months.	Flap.	Lower third.	Recovery in 5½ wks.	Slight sloughing.
16.....	M.	34	Tubercular knee.....	2 years.	Flap.	Middle.	Death in 4 days.	Exhaustion. Pus had dissected up along femur.
17.....	M.	19	Osteo-sarcoma of femur.....	5 months.	Flap.	Middle.	Recovery in 6 wks.	

18.....	M.	18	Osteo-myelitis of femur..	11 years.	Flap.	Upper third.	Recovery in 6 wks.	Small sinuses (two).
19.....	M.	19	Osteo-sarcoma of femur.....	10 months.	Flap.	Middle.	Recovery in 6 wks.	One stitch-abscess.
20.....	M.	29	Tubercular knee. Anchylosis.....	Life.	Flap.	Lower third.	Recovery in 6 wks.	Slight sloughing of flaps.

Amputations at Knee-Joint. (Traumatic, Primary.)

1.....	M.	25	Crushed leg.	Recent.	Flaps.	.....	Recovery in 6 wks.	Slight sloughing of flaps.
2.....	M.	46	Crushed leg.....	Recent.	Flaps.	.....	Recovery in 4½ wks.	Slight sloughing of flaps.

Amputations of the Leg. (Traumatic, Primary.)

1.....	M.	6	Compound fracture of tibia and fibula.....	Recent.	Mixter.	Lower third.	Recovery in 7 wks.	Fracture of both arms.
2.....	M.	7	Laceration and crush of foot.....	Recent.	Flap.	Middle.	Recovery in 6 wks.	
3.....	M.	11	Compound comminuted fracture of fibia and tibula.....	Recent.	Flap.	Middle.	Recovery in 10 wks.	Fracture of other leg, also.
4.....	M.	14	Compound fracture of tibia and fibula.....	Recent.	Flap.	Middle.	Recovery in 6 wks.	Slight sloughing of flaps.
5.....	M.	11	Compound fracture of tibia and fibula.....	Recent.	Flap.	Upper third.	Death in 4 days.	Exhaustion. Shock. Severe multiple injuries.
6.....	M.	10	Crushed foot.....	Recent.	Flap.	Lower third.	Recovery in 4 wks.	
7.....	M.	29	Compound fracture of tibia and fibula.....	Recent.	Flap.	Middle.	Recovery in 7 wks.	Some suppuration.

Amputation of the Leg. (Traumatic Primary.) — *Continued.*

No.	Sex.	Age.	Nature of Injury.	Duration.	Methods.	Place.	Result.	Remarks.
8.....	M.	28	Compound fracture of tibia. Laceration.....	Recent.	Flap.	Upper third.	Recovery in 11 wks.	Severe general injuries.
9.....	M.	31	Crushed foot.....	Recent.	Flap.	Lower third.	Recovery in 2 wks.	
10.....	M.	27	Crushed leg.....	Recent.	Flap.	Upper third.	Recovery in 6 wks.	Drained on account of the laceration.
11.....	M.	7	Crushed Leg.....	Recent.	Flap.	Upper third.	Recovery in 5 wks.	Some sloughing of flaps,
12.....	M.	14	Compound fracture of tibia and fibula.....	Recent.	Flap.	Upper third.	Recovery in 4 wks.	Laceration of other leg.

Amputations of the Leg. (Traumatic, Secondary.)

1.....	M.	37	Compound comminuted fracture of fibula.....	3 weeks.	Flap.	Middle.	Recovery in 7½ wks.	Some suppuration.
2.....	M.	64	Compound comminuted fracture of tibia and fibula.....	5 days.	Flap.	Lower third.	Recovery in 9 wks.	Some sloughing of flaps.
3.....	M.	38	Crushed foot. Gangrene.....	3 weeks.	Flap.	Lower third.	Recovery in 3 wks.	
4.....	F.	3	Compound fracture of metatarsus.	2 weeks.	Flap.	Lower third.	Recovery in 4 wks.	
5.....	M.	22	Compound fracture of tibia and fibula.....	6 days.	Flap.	Middle.	Death in 10 days.	Pneumonia. Gangrene.
6.....	M.	adult	Compound comminuted fracture of both bones.....	5 days.	Flap.	Upper third.	Recovery in 4 wks.	Phthisis.
7.....	M.	21	Traumatic necrosis of tarsus.....	11 weeks.	Flap.	Upper third.	Recovery in 3 wks.	
8.....	M.	34	Compound fracture of tibia and fibula.....	10 weeks.	Flap.	Middle.	Recovery in 6 wks.	Some sloughing of flaps.
9.....	M.	23	Sloughing of stump. Cause, trauma.....	1 month.	Flap.	Middle.	Recovery in 2 mos.	Vide double amputations, No. 2.

Amputations of the Leg. (Pathological.)

1	M.	12	Tubercular foot	1 year.	Flap.	Lower third.	Recovery in 3 mos.	Had suppurating sinus of foot. Abscess formation in stump.
2	M.	24	Tubercular ankle	8 months.	Flap.	Lower third.	Recovery in 6 wks.	
3	M.	69	Gangrene of foot	6 weeks.	Flap.	Middle.	Recovery in 9 wks.	Some sloughing of flaps.
4	M.	21	Abscess of amputation stump (seven years)	10 days.	Flap.	Upper third.	Recovery in 9 wks.	Suppuration.
5	M.	66	Diabetic gangrene of toe	1 year.	Flap.	Upper third.	In Hospital.	Doing very well.

Amputations at Ankle-Joint. (Traumatic, Primary.)

1	M.	8	Crushed foot	Recent.	Flap.	.....	Recovery in 7 wks.	Crush of other foot, also.

Double Amputations.

1	M.	38	Compound fracture of both forearms	Recent.	Flap.	Upper third, middle.	Recovery in 3½ wks.	
2	M.	23	Crushed feet	Recent.	Flap.	Ankle-joint, middle.	Recovery in 3 mos.	Vide amputations of leg (traumatic, secondary). No. 9.

STATISTICS OF THE MAJOR AMPUTATIONS (SEVENTY-SIX) AT THE BOSTON CITY HOSPITAL. (1894–NOV. 1, 1897.)

Place.	Traumatic, Primary.				Traumatic, Secondary.				Pathological.				Grand Total.			
	Recovered.	Died.	Total.	Per cent. of Mortality.	Recovered.	Died.	Total.	Per cent. of Mortality.	Recovered.	Died.	Total.	Per cent. of Mortality.	Recovered.	Died.	Total.	Per cent. of Mortality.
Hip	....	....	....	.....	....	....	....	.....	...	1	1	.....	....	1	1	
Thigh	2	2	4	50.00	3	1	4	25.00	17	3	20	15.00	22	6	28	21.43
Knee	2	....	2	.....	....	....	....	.....	....	....	....	.....	2	....	2	
Leg	11	1	12	8.33	8	1	9	11.11	5	....	5	.....	24	2	26	7.69
Ankle	1	....	1	.....	....	....	....	.....	....	....	....	.....	1	....	1	
Shoulder	....	....	....	.....	1	....	1	.....	....	....	....	.....	1	....	1	
Arm	3	....	3	.....	2	....	2	.....	2	....	2	.....	7	....	7	
Elbow																
Forearm	4	....	4	.....	3	....	3	.....	1	....	1	.....	8	....	8	
Total	23	3	26	11.54	17	2	19	10.53	25	4	29	13.79	65	9	74	12.16
Double Amputations.																
Forearms	1	....	1	.....	....	....	....	.....	....	....	....	.....	1	....	1	
Legs	1	....	1	.....	....	....	....	.....	....	....	....	.....	1	....	1	
Total	25	3	28	10.71	17	2	19	10.53	25	4	29	13.79	67	9	76	11.84

Seventy-six amputations, representing 12,744 surgical admissions, or .591%.

STATISTICS OF THE MAJOR AMPUTATIONS (368) AT THE BOSTON CITY HOSPITAL. (1864–1880.)

By Herbert L. Burrell, M.D.

Hip	....	3	3	100.00	....	....	....	.....	....	1	1	.....	....	4	4	
Thigh	21	37	58	63.00	8	8	16	50.00	24	9	33	27.02	53	54	107	50.47
Knee	4	3	7	42.85	....	3	3	... ..	3	....	3	.....	7	6	13	46.15
Leg	29	15	44	34.09	12	4	16	25.00	30	8	38	21.05	71	27	98	27.55
Ankle	6	2	8	25.00	6	....	6	.....	8	1	9	11.11	20	3	23	13.04
Shoulder	10	8	18	44.44	1	1	2	50.00	1	....	1	.....	12	9	21	42.86
Arm	27	9	36	25.00	5	6	11	54.54	10	1	11	9.09	42	16	58	30.77
Elbow	1	....	1	.....	....	....	....	.....	1	....	1	.....	2	....	2	
Forearm	21	1	22	4.54	6	2	8	25.00	1	2	12	16.7	37	5	42	11.96
Total	119	78	197	39.59	38	24	62	38.71	87	22	109	20.18	244	124	368	33.70

Three hundred and sixty-eight amputations, representing 17,815 surgical admissions, or 2.01%.

STATISTICS OF THE MAJOR AMPUTATIONS (369) AT THE BOSTON CITY HOSPITAL. (1880–NOV. 1, 1897.)

By J. T. Bottomley, M D.

Place.	Traumatic, Primary.				Traumatic, Secondary.				Pathological.				Grand Total.			
	Recovered.	Died.	Total.	Per cent. of Mortality.	Recovered.	Died.	Total.	Per cent. of Mortality.	Recovered.	Died.	Total.	Per cent. of Mortality.	Recovered.	Died.	Total.	Per cent. of Mortality.
Hip	....	....	....	.....	....	....	....	.....	7	3	10	30.00	7	3	10	30.00
Thigh	8	6	14	42.86	8	4	12	33.33	55	14	69	20.29	71	24	95	25.26
Knee	4	1	5	20.00	1	1	2	50.00	3	....	3	.....	8	2	10	20.00
Leg	48	8	56	14.29	28	5	33	15.15	47	5	52	9.62	123	18	141	12.76
Ankle	8	....	8	.....	2	1	3	33.33	4	1	5	20.00	14	2	16	12.50
Shoulder	5	3	8	37.50	1	....	1	.....	2	1	3	33.33	8	4	12	33.33
Arm	18	3	21	14.28	6	2	8	25.00	9	2	11	18.18	33	7	40	17.50
Elbow	1	....	1	.....	....	...	....	.....	2	....	2	.....	3	....	3	
Forearm	19	...	19	.....	6	2	8	25.00	10	....	10	.....	35	2	37	5.41
Total	111	21	132	16.00	52	15	67	22.39	139	26	165	15.76	302	62	364	17.03

Double Amputations.

Forearms	1	1	2	50.00	...	....	....	.....	....	...	....	.....	1	1	2	50.00
Legs	2	1	3	33.33	....	....	....	.....	....	....	....	.....	2	1	3	33.33
Total	114	23	137	16.79	52	15	67	22.39	139	26	165	15.76	305	64	369	17.34

Three hundred and sixty-nine amputations, representing 44,970 surgical admissions or .821%.

VIII.

THE CLINICAL AND PATHOLOGICAL REPORT OF A CASE OF FRACTURE OF THE SPINE IN THE CERVICAL REGION WITH SOME STATISTICS ON FRACTURES IN THIS REGION.

By J. W. Courtney, M.D.

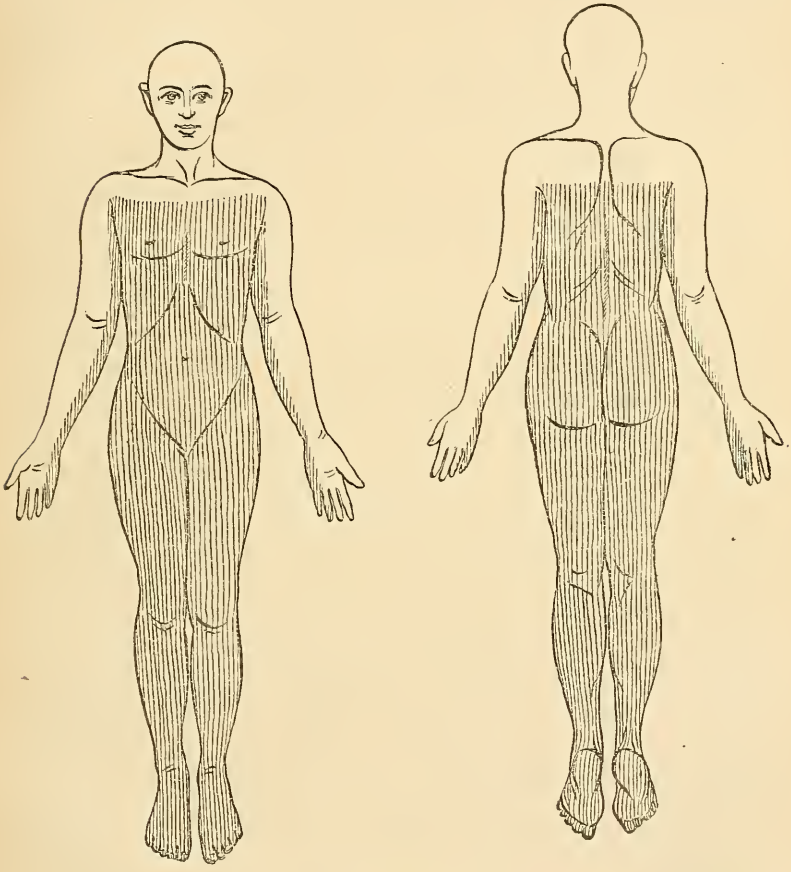
The case about to be reported is offered for two reasons: First, because of the interesting pathological findings brought to light by the careful and exhaustive microscopic examination of Dr. J. J. Thomas, and second, as a contribution to the study of the patellar reflexes in lesions of this kind.

The patient was first seen by me in consultation with Dr. R. W. Lovett, on October 2 of this year at the Boston City Hospital, where he had been admitted with the diagnosis of fracture of the spine. The question was as to the justifiability of operative interference.

The complete history of the case was as follows: The patient was forty-three years of age, single, and a sailor by occupation. His family history was unimportant. Previous history: Periodic excessive indulgence in alcohol; gonorrhœa six or seven times, chancre two years previously without secondaries. Present illness: On the day before admission, at about five o'clock in the afternoon, and seventeen hours before I saw him, he had, while drunk, fallen down a flight of twelve steps, striking on his back and shoulders. He was rendered unconscious by the fall and remained so for about half an hour. When he came to, he could not move his lower extremities at all, and his upper only partially. Up to the time of admission he had not passed any urine and his bladder was found much distended, requiring catheterization.

Examination showed a man, muscular and well-nourished. He was lying on his back with face flushed and somewhat cyanotic. Pysche clear. The pupils were small, regular and equal, and did not react to light or in accommodation.

The cranial nerves were not involved. The movements of the head were limited in all directions, owing in part to pain in neck and shoulders. There was no marked deformity in the spine, but I thought I detected an abnormal lateral mobility of a spinous process in the lower cervical region. To this, however, Dr. Lovett could not agree. In the upper extremities the only movements possible were elevation, depression



and abduction of arms and flexion of forearms. The patient could not pronate or supinate, move the wrist, abduct or adduct the fingers, and the grasp was nil. Fibrillary tremor was marked in the biceps on both sides. Breathing was almost wholly diaphragmatic. Heart sounds and area were apparently normal and the lungs thus far free. Pulse sixty. Respiration twenty-five. Temperature ninety-seven. The

lower extremities were completely paralyzed, the patellar reflexes entirely abolished, as likewise the superficial except a slight plantar reaction on the right. Sensation was absent over the entire lower extremities and trunk up to a point corresponding to the upper border of the second rib in front; in the arms the anesthesia corresponded — as diagram shows— to the region supplied by the internal cutaneous and ulnar nerves.

As to the location of the greatest height of the cord lesion the distribution of the paralysis and anesthesia in the arms was, of course, the index. It will be remembered that the paralysis here corresponded to the lower-arm type and hence involved no nerve which arises higher than the seventh cervical segment; the cutaneous disturbance corresponded to the areas supplied by the ulnar and internal cutaneous, which take their origin from the seventh and eighth cervical and first dorsal nerves. The contracted and fixed pupil also pointed to a disturbance at the level of the first dorsal nerves. From the topographical relation of these nerves to the vertebrae I concluded that the mischief to the spine was, in its highest point at the level of the spinous process of the sixth cervical vertebra, and from the condition of the spine — absence of marked deformity — that the lesion was more probably fracture than dislocation. Furthermore from the absence of the knee-jerks I ventured the conclusion that the cord lesion was absolutely transverse — a deduction which put operative interference totally out of the question.

The next day (October 3) the patient's condition was nearly the same except that temperature, pulse and respiration had risen. He required constant catheterization, and priapism was always noted at such times. He felt fairly comfortable and took some liquid nourishment.

October 4. Pulse and temperature still going up. Patient soporous.

October 5. Cyanosis of face deeper. General condition about the same. Pupils still small, equal and fixed; paralysis, reflexes and anesthesia the same as before.

October 6. Patient very soporous. Face perspiring. Coarse bubbling râles at both bases, especially at right. Breathing more and more difficult, and entirely diaphragmatic. Slightly delirious in P.M. Kept elevating and depressing arms as if to aid in breathing.

October 7. Died at 12.10 A.M., about six days after onset.

The report of the autopsy, which was performed four days later by Dr. Mallory, enabled me to explain the mechanism of the damage to the cord. It read as follows: "Body that of a man about fifty years old. 130 cm. long. Abdominal pleural and pericardial cavities normal.

Heart, weight, 365 grammes. Right side normal. Left side, wall somewhat thickened and left ventricle slightly dilated. Valves and cavities normal. Teased preparations show slight fatty changes.

Lungs, both lungs very dark in color and very dense to touch. Bloody fluid could be squeezed from cut surface. There were also irregular darkly mottled portions with hemorrhagic appearance.

Liver, weight, 480 grammes. Pale in color and firm to touch. Lobulations not distinct.

Spleen, weight, 165 grammes, of ordinary size, dark red in color; malpighian bodies not distinct. Pulp not increased.

Kidneys, weight, 360 grammes. Both were large and dark red in color. Cortex not increased. On teasing, no fatty change.

Stomach and intestines normal.

Larynx, trachea and testicles normal.

Pancreas, adrenal glands, bladder and prostate normal.

Aorta showed slight yellowish areas. Brain, weight, 1,190 grammes. Normal.

Cord: Examination of spinal column from the anterior surface showed a transverse fracture of the body of the seventh cervical vertebra. On the left side there was slight hemorrhage in the tissue adjoining the body of the vertebra; only small fragments projected into the tissue. A small hole on the left side led down towards the spinal canal. On examination of the vertebral column from the back, quite a little hemorrhage was found in the muscles surrounding the lower cervical vertebrae.

The posterior portion of the arches of the sixth and seventh cervical vertebrae were broken into several pieces, and projecting into the adjoining muscles which had been lacerated by them. On the posterior surface of the dura, beneath the posterior arch of the seventh cervical vertebra

and, to a less extent, beneath that of the sixth was a small amount of dark reddish, coagulated blood. On opening into the cord no sign of hemorrhage was found within the dura. The blood vessels on the surface of the cord were injected. Although the cord was partially frozen, and small spiculae of ice lay within the spinal canal, very distinct softening of the cord opposite the point where the sixth cervical nerve was given off could be felt.

ANATOMICAL DIAGNOSIS.

Hypertrophy of left ventricle. Hemorrhage in lungs, Slight arterio-sclerosis. Fracture of sixth and seventh cervical vertebra. Softening of cervical cord opposite the sixth nerve.

CULTURES.

Heart, kidney, liver and spleen, sterile.

The sixth segment of the cord, it will appear from these findings, owed its softening in all probability to the jamming upwards and forwards of the fragments of the broken arch of the sixth vertebra, which were immediately retracted by their ligamentous and muscular attachments. In this connection the absence of pressure from bony fragments, of dislocation, and of any great amount of intra or extra dural hemorrhage is significant when viewed from an operative standpoint.

What remained to be cleared up was the absence of any symptoms, clinically, referable to the sixth nerve, which ought from the seat of the intense softening in the sixth segment, to have been involved. On this point Dr. Thomas' findings were important.

The cord was removed, and hardened by him in a ten per cent. solution of formalin. Sections were made first at the point of greatest softening, *i.e.*, at the sixth cervical segment; again at the level of the second cervical segment, at the sixth dorsal segment, and at the second lumbar segment.

The stains used were hematoxylin and eosin; Van Gieson's picric acid and acid fuchsin stain for the central nervous system; eosin and Unna's alkaline methylene blue stain; and Marchi's method. The section at the level of the sixth cervical segment showed no changes in the nerve roots, either

anterior or posterior. The pia was slightly thickened, and in one spot near the point of exit of an anterior nerve root there was an area infiltrated with small round lymphoid cells with round deeply stained nuclei, surrounded by a narrow zone of clear protoplasm. There were also occasional leucocytes and larger cells with irregular nuclei not staining deeply, with more protoplasm surrounding the nuclei, the protoplasm having a faint bluish tinge in the section stained with alkaline methylene blue. Occasional red blood globules were found in this region. In the white matter of the cord at this level the small blood vessels were filled with red blood globules and some of them were widely dilated. About many of them there was a small infiltration of lymphoid cells and leucocytes. Throughout the white matter there were scattered red blood globules, and in various places there were numerous larger and smaller hemorrhages, some near small blood vessels and some at a distance from any blood vessel. Scattered through the white substance also, but more numerous at the periphery of the cord about the blood vessels and in the neighborhood the small hemorrhages, there were numbers of large cells from two to eight times the size of a leucocyte. These cells had moderately large, irregular, granular nuclei, not staining deeply. Some of the cells contained two nuclei, and in others the nucleus was in two parts connected by a rather thin band. The protoplasm of these cells was finely or coarsely granular. In the sections stained according to Marchi's method it was seen that many of these cells contained fat globules of various sizes. Other cells showed the granular appearance, but the granules were not stained by the osmic acid. Occasionally a red blood globule was seen enclosed in one of these large leucocytes. The nerve structures of the white substance of the cord were separated by the hemorrhage and the exudation into them, but looked fairly normal. In the sections stained by Marchi's method, however, it was seen that in many cases the axis cylinder was replaced by a round globule of fat, and even the myelin sheath had also undergone fatty degeneration, and only a large black mass could be seen. In others the axis cylinder had disappeared and the myelin sheath was represented by a complete, or broken, ring of fat. These changes were about equally well marked in all parts of the

white substance. Throughout this part of the cord were rounded, irregular, sometimes elongated, masses staining homogeneously with the hematoxylin and eosin stain, which were apparently masses of myelin, and some of the large leucocytes contained these same homogeneously stained masses. In the gray matter of the cord much the same condition was found, except that here the hemorrhages were more numerous and larger, and the amount of exudation greater. The large phagocytic leucocytes were also quite numerous throughout this area, more especially in the anterior horns, and rather less in the posterior horns. The irregular masses and bands of myelin were present also, chiefly in the anterior horns. The large ganglion cells of the anterior horns had retained their shape fairly well, in some instances remarkably so. The nucleolus, however, showed only as a slightly more darkly staining body within the cell, and almost without exception the cells showed more or less fatty degeneration. In some cells there were a few scattered fat globules, in others the whole cell body appeared filled with the small black granules. In other cells where black granules were massed in only one part of the cell they were probably in large part the pigment granules of the cells. The fat globules in the large leucocytes in the gray matter of the cord seemed rather greater in number than in those in the white substance. The bands and irregular masses of protoplasm also showed in places the presence of fatty degeneration.

The sections at the level of the second cervical segment showed very slight changes. In one, in the white substance, just at the border of the lateral horn of gray matter, there was a small hemorrhage. There was, also, all through the white substance of the cord a slight degeneration of the nerve fibres shown by the replacing of the axis cylinder, or of the myelin sheath, by fat, while many of the nerve fibres were much swollen. This was seen in all parts of the white matter, but was greatest in the crossed pyramidal tracts and the posterior tracts. The large nerve cells of the anterior horns contained rather an unusually large amount of pigment and occasionally the nucleolus and protoplasmic granules stained fairly, but in most of the cells these substances appeared normal. The membranes and nerve roots showed no changes.

The sections from the dorsal region of the cord showed much the same condition as that found in the upper cervical region. Considerable numbers of nerve fibres in the white substance were degenerated, the axis cylinder or myelin sheath being replaced by fat. Swollen fibres were also present in moderate numbers. Here again the changes were most marked in the crossed pyramidal tract and posterior columns. The nerve cells of the anterior horn, in sections stained by Marchi's method, showed numerous black granules, some of the cells being completely filled with them. In other cells they were massed together in one part of the cell only. These granules were probably in part the pigment granules of the cell, and in part globules of fat. In these cells, also, as in those of the upper cervical cord, the nucleolus and protoplasmic granules were usually distinct, but in some they stained very faintly with the alkaline methylene blue stain. In the anterior nerve roots there were a few fatty degenerated nerve fibres.

In the lumber region of the cord there was the same diffuse degeneration of nerve fibres in the white substance, and quite numerous large swollen nerve fibres. The changes again were most marked in the lateral pyramidal and posterior tracts of the cord, and were here, if anything, more marked than in the dorsal cord. The anterior nerve roots showed a few degenerated nerve fibres, and the nerve cells of the anterior horn showed changes similar to those found in the dorsal cord. Many of the cells were completely filled with small black granules.

Diagnosis: Hemorrhage and acute transverse degeneration at the level of the sixth cervical segment of spinal cord.

Acute diffuse degeneration of nerve fibres of lateral pyramidal tract and of posterior columns.

Slight acute degeneration of ganglion cells of anterior horn of dorsal and lumbar regions of cord and of anterior nerve roots of these regions.

There are many interesting features in connection with these findings, notably the complete transverse character of the lesion in the sixth cervical segment with escape of the sixth nerves. Of great practical significance in connection with operative interference are the intense secondary degen-

erative changes which had taken place throughout the cord in less than six days, and, finally, of physiological interest is the *descending* (?) degeneration which was noted in the posterior columns. This latter condition is now a matter of fairly common observation, and various hypotheses have been put forward to account for its existence, but none of them is satisfactory. Bruns[1] considers it to be a degeneration of the so-called descending fibres of the posterior roots, and quotes Marie as his authority. Tooth[2] has shown that cutting of the posterior nerve roots alone does not produce this descending degeneration and that the latter extends lower than the descending collaterals of the posterior roots. In support of Tooth's views stand those of Gombault and Philippe[3] who in one case by destruction of the posterior roots alone got no descending degeneration and in another by total cross section of the cord succeeded in getting it. They concluded, however, that they were dealing with commisural fibres of no great length. From this last conclusion Egger[4] dissents because in a case of complete transverse destruction of the cord from fracture in the upper dorsal region, he found extensive secondary degeneration in the posterior columns both horizontally and *vertically*.

As a possible explanation of the phenomenon, I offer the following: Bruns[5] noted in his case that the lateral pyramidal tracts directly under the lesion were strikingly normal, whereas low down in the cord they were much degenerated, and in explanation of this he says that degeneration begins first in the most distal portion of a cut nerve and reaches the end nearest the lesion last of all. In our case, Dr. Thomas noted that the changes in both the pyramidal tracts and posterior columns were, if anything, more marked in the lumbar region than in the dorsal, a circumstance which not only supports Bruns' theory as regards the modus operandi of pyra-

[1] L. Bruns, Ueber einen Fall totaler traumatischer Zerstörung des Rückenmarkes an der Grenze zwischen Hals und Dorsalmark. Archiv. für Psychiatrie und Nervenkrankheiten. Band xxv., S., 808.

[2] Tooth, Secondary degeneration of the spinal cord. London, 1889.

[3] Gombault and Philippe, Contribution à l'étude des lésions systématisées dans les cordons blancs de la moelle épinière. Archives de médecine expérimentale. No. 3, 1894.

[4] F. Egger, Ueber totale Compression des oberen Dorsalmarkes. Archiv. für Psychiatrie und Nervenkrankheiten. B. xxvii., S 129.

[5] Bruns, loc. cit.

midal degeneration, but allows the inference that the same theory may hold good for the posterior column, and that the paradox of descending degeneration of this column is merely apparent and not real. I do not, however, insist on this point.

To return once more to the clinical side of the case: Does the absence of the knee-jerk in fractures of the cervical and — for that matter — of the upper dorsal spine signify a total transverse lesion of the cord? This is a question which has engaged the attention of all observers since Bastian[1] made special mention of the subject in 1882. Bastian was not, however, according to Egger,[2] the first to call attention to the phenomenon, although he was probably the first to attempt an explanation of it. Kadner[3] in 1876 published a case of carcinoma of the first four dorsal vertebrae in which the reflexes were lost and remained so until death occurred, nineteen days after the complete establishment of paraplegia. The pathological examination showed complete atrophy of the cord at the height of the second dorsal vertebra. The same author observed the absence of the knee-jerk in a second case also, which was one of fracture, but referred to it only briefly, stating that it was opposed to the results obtained experimentally on animals.

Bastian's explanation that it is due to the cutting off of the paths from the cerebellum, namely, the direct cerebellar tracts — which have to do with the maintenance of muscle tonus — has received support from such observers as have noted the absence of the knee-jerks in cerebellar tumors. The opponents of this theory point out its untenability on the ground that there are no descending fibres from the cerebellum to the cord. Oppenheim[4] came out very strongly in '94 with the statement that the absence of the knee-jerk had never been observed by him in uncomplicated cerebellar tumor, and that it meant a co-existing disease of the posterior columns of the cord. He further[5] very pointedly recommends future investigators to

[1] H. C. Bastian in Quain's Dictionary of Medicine, p. 1480. 1882. Also later article on the Symptomatology of Total Transverse Lesions of the Spinal Cord; with special reference to the condition of the various reflexes. Medico-Chirurgical Transactions. London, 1890, p. 150 *et seq.*

[2] Egger, loc. cit.

[3] Kadner, Zur Casuistik der Rückenmarks compression. Wagner's Archiv. der Heilkunde, 1876.

[4] H. Oppenheim, Sitzungsbericht der Berliner Gesellschaft für Psychiatrie und Nervenkrankheiten. Neurol. Centralbl. 1894, No. 1.

[5] Same author. Die Geschwülste des Gehirns. Wien, 1893.

examine the cord as well as the brain in those cases of cerebellar tumor where the phenomenon of absent knee-jerk is observed clinically.

Sternberg[1] offers the hypothesis of an inhibitory influence which starts from the point of the lesion and acts upon the centres below. It requires, however, as Egger[2] justly says, a considerable effort of the imagination to understand how this vague inhibiting power can be active for any great length of time.

Shock has also been offered as an explanation. To this Egger again objects on the ground that the clinical picture of shock is too characteristic and its duration too definite to attempt to make the phenomenon in question a part. In connection with this I might add that in one case of fracture which I obtained from the hospital records in which a severe lesion to the cord was undoubtedly present, the knee-jerks were noted as present during the first twenty-four hours (period of greatest shock) after the injury, and later as absent.

Whatever the explanation of the matter may be, it suffices to say that there are now on record a fairly large number of carefully (both clinically and microscopically) observed cases in which the absence of the knee-jerk has been noted in total transverse lesions of the cervical and upper dorsal cord. In only thirteen out of fifty cases of fracture in the cervical region of the spine, whose reports I examined in the City Hospital records, was the condition of the reflexes noted, but in all thirteen there was complete absence of the knee-jerk, once with preservation of slight cremasteric reflex, and once with slight plantar. In my own case the plantar reflex was slightly present on the right.

In concluding this portion of the paper, I will say that I draw no sharp general conclusions from the behavior of the knee-jerks in my case, but simply offer the observation as so much positive evidence.

As to the general subject of fractures in the cervical region of the spine, the following facts elicited by an examination of the records of this hospital need no comment. Of the

[1] Sternberg, M., Die Reflexe und ihre Bedeutung für die Pathologie des Nervensystems, 1893.

[2] Egger, loc. cit.

158 cases of fracture of the spine admitted to the hospital from January, 1881, to May, 1897, fifty were in the cervical region, and of these fifty all died. I have classified them as to topographical distribution and to duration of life after accident as follows:

		Duration.	Av. Duration.
Upper cervical region,	1 case,	24 hours,	——
Middle " "	9 cases,	Few hours to 1 day.	18 hours.
Lower " "	40 "	" " " 1 month.	5 days.

In twenty-three cases there was no deformity or crepitus. In fifteen these were not mentioned. Deformity, when present, was usually in the nature of slight depression and abnormal mobility. Crepitus was noted only three or four times. Tenderness over the injured area of the spine was, on the contrary, a common observation.

Five cases were operated. In none were the fragments found to be pressing on the cord. In two there was special mention made of the fact that no extra or intra-dural hemorrhage was manifest. One case died on the table, and one in forty-eight hours.

Only three autopsies appear in the records. The first stated that the cord was softened and red and that the fractured vertebra was not pressing upon it. No extra or intra-dural hemorrhage was found.

Autopsy number two showed slight anterior displacement of the fractured vertebra and only a moderate amount of blood outside and within the dura. Complete disintegration of cord at point opposite fracture. Fragments not pressing on cord.

Autopsy number three showed fracture of the spinous process of the sixth cervical vertebra, with separation between this process and that of the fifth admitting tip of little finger. There was also a displacement of the fifth vertebra forward to the extent of nearly one-quarter inch. In the spinal canal within this lesion the dura was reddened, but there was no free blood either outside or inside the meninges. In immediate relation with the vertebral injury the cord showed an area of softening through one-half inch of its length and involving its entire thickness. The cord was at this point of the consistency and color of thick cream. There was no hemorrhagic appearance.

IX.

TREATMENT OF PROLONGATION FORWARD OF THE NASAL SEPTUM INTO THE NOSTRIL.

By John W. Farlow, M.D.

There have come under my care a number of cases presenting a form of abnormality of the nasal septum which caused marked discomfort, but which has received almost no mention in text books on the nose and throat. This is a marked elongation of the cartilaginous septum and projection of its anterior end into one nostril. Instead of remaining in the median line just behind the fleshy septum, its extra length causes it to bend forward into the opening of one nostril, thus pushing the fleshy septum to the other side.

There are three principal symptoms which I have found connected with this condition:

First. Nasal obstruction, caused by the narrowing or blocking of the nostril by the superfluous cartilage. There may be almost complete occlusion and where the ala of the nose has a tendency to fall in, as is often the case where nasal respiration is impeded, or where secretion and crusts gather behind this obstruction, we have the conditions present which give rise to catarrh, mouth breathing, eustachian closure, etc.

Second. Congestion, dilated capillaries, cracks, fissures, tendency to bleed, eczema of the opening of the nostril. The sharp, thin edge of the overgrown cartilage pushes the fleshy septum to one side and thrusts before itself the mucous membrane and skin of the entrance to the nose, putting it greatly on the stretch, like a too small amputation flap over a sharp edge of bone. The consequence of this tension is a congestion of the soft parts immediately in front of the aggressive cartilage. Then come cracks, fissures and inflammation in the form of eczema and hypertrophy of the surround-

ing parts. The irritation and itching lead to constant rubbing, blowing and wiping of the nose as well as sniffing and other movements, all of which tend to make matters worse. Salves and washes serve only a temporary purpose where the cause remains.

Third. The appearance of the nose. The growth of the septum into one nostril gives a bent look to the tip of the nose. The thickened skin and dilated vessels, and especially the cracks and fissures are often quite enough to demand treatment, even when the nostril is not blocked up. Women, in particular, are very anxious to be rid of what is a decided and conspicuous blemish. So that for aesthetic reasons alone an operation may be advisable.

As regards treatment, removal of enough of the anterior end of the cartilage to relieve the tension under the skin, and, in case the nostril is occluded, to cut off enough to allow free respiration is the object to be attained. If the skin at the opening of the nostril is cracked or covered with crusts, it is well to use a cleansing wash and protective ointment, in order to make the skin soft and healthy as a preliminary to operation.

Cocaine applied to the mucous membrane renders the operation painless. An incision should be made through the mucous membrane, parallel with the free edge of the septum and near enough to it so that the perichondrium can be stripped back from the cartilage on both sides through one incision. After the mucous membrane and perichondrium are cut through, these tissues are pushed back from the cartilage. The latter is then trimmed off with a knife or scissors until enough has been removed to relieve the pressure under the skin and free the nostril. Care should be taken to cut down well toward the floor of the nose where is the bony support of the bottom of the septum. It is sometimes well to remove a portion of the thickened skin.

The septum may deviate higher up into the other nostril, or the deviation and prolongation may be in the same nostril. In the latter case, after shortening the septum, it is well to make several cuts into the cartilage at right angles to the original incision, or even remove a triangular piece from the cartilage to reduce its size and elasticity, and allow it to be

pushed to the other side, where it can be held by a plug till healing has taken place.

After stopping the bleeding, which is generally moderate, bathing the wound, bringing the edges together and applying aristol or other powder, a stitch can be taken, to remain two or three days till the parts are united, or a pledget of gauze alone may be enough to keep the parts in contact by pressure till they are healed.

If the operation has been successful the tip of the nose no longer bends to one side; the fleshy septum is under the end of the cartilage, the thickened, congested tissues become normal, the cracks disappear, the irritation ceases and nasal respiration is restored.

X.

A CASE OF VESICO-UTERO-VAGINAL FISTULA, TREATED BY COLPOCLEISIS.

By Charles M. Green, M.D.

M. G., aged forty-two, married, entered the hospital, Oct. 2, 1896, with the following history:[1] her fifth labor had occurred Sept. 6, 1896; it was instrumental, the child being still-born, and ever since the delivery urine had dribbled from the vagina. For nearly four weeks she had lain in bed uncared for. The buttocks were covered with bed-sores, the general condition was very poor, and the nervous system unstrung. The vulva and vagina were excoriated and reddened, the vaginal walls encrusted with phosphatic deposits, and the vault was a mass of sloughing tissue. High up could be felt a vesical fistula, the exact relations of which could not then be determined.

Two weeks were spent in restoring the patient's general health, healing the bed-sores, arresting the necrosis about the fistula, and removing the phosphatic deposits from the bladder and vaginal walls. Various measures were tried for the latter purposes; but the most effectual treatment was the following: salol and boracic acid were given internally, with diluent drinks; bladder and vagina were irrigated with two per cent. boracic acid solution; the vaginal vault was thoroughly swabbed with hydrogen peroxide, again irrigated, and then dressed with cotton wetted with one-fifth per cent. hydrochloric acid. The bladder was also irrigated with the same strength of hydrochloric acid. The sloughs that came away were found to be composed of loose unstriped muscle and connective tissue.

October 28, a careful examination was made under ether. The uterus was high in the pelvis, and firmly fixed. The

[1] Gynaecological Records, Vol. 24, page 305.

posterior cervical lip had partially sloughed away, the anterior infra-vaginal cervix entirely so. The fistula, which was between three and four cm. in diameter, was held immovably in the cicatrix of the vaginal vault, and the upper border could not be drawn down within easy view. The left ureteral orifice was one-half inch below and to the left of the fistula, the right, one-fourth inch below and to the right. The bladder was contracted and its walls thickened; but the mucosa looked healthy. The upper border of the fistula was densely adherent to the uterine wall. The posterior surface of the vagina looked normal and free from cicatrix.

It seemed obvious that this case belonged to the so-called inoperable class — inoperable, that is, by the usual, comparatively simple, methods. Several operative measures have been proposed for the treatment of these "inoperable" cases, and these were duly considered in this case before resort to closure of the vagina. Dittel, in 1893, proposed in such cases to reach the fistula from above, by abdominal incision — freeing the bladder from the uterus and vagina, closing the fistula and replacing the bladder, and then reuniting the vesico-uterine peritoneum. Mackenrodt, in 1894, suggested the following operation for the closure of large fistulae: The border of the fistula is split, and the bladder dissected entirely free from the vagina and uterus; the bladder being thus freed is easily drawn together, and the margins of the fistula united with sutures; the vaginal wound is then approximated as far as may be, the body of the uterus being drawn forward into anteversion and included in the vaginal suture.

In the Johns Hopkins Bulletin for February-March, 1896, Kelly proposes a modification of Mackenrodt's operation, as follows: The bladder is dissected away from the anterior uterine wall, and the freed upper border of the fistula is then easily brought into apposition with the lower border: the body of the uterus is not included in the vaginal closure.

No one of the above-mentioned methods seemed applicable in the case reported, owing to the dense, cicatricial connection between the bladder and the uterus, and owing further to the fixation of the uterus, which greatly impeded manipu-

lation. It was therefore decided to close the vagina, after the nature of the operation had been explained to the patient and her husband, and their consent obtained. A denudation, one-half inch in width, was made around the vagina, the posterior border beginning high up, just below the posterior cervical lip, and the anterior just below the lower border of the fistula: the vagina was then drawn together with ten silkworm-gut sutures, so passed as to approximate the anterior and posterior walls. The convalescence was uneventful. For a time a catheter was kept in the bladder for drainage, and the bladder was occasionally irrigated. The stitches were removed in two weeks, at this time the patient having complete control of her bladder: there was no vaginal leakage of urine after the operation. On discharge from the hospital, twenty-four days after operation, the vaginal union was firm, vesical continence complete, and although the vagina was somewhat shortened, it was of sufficient length to admit of coitus.

The operation of colpocleisis is manifestly open to certain objections. As stated by Pozzi, these objections are:

1. That fecundation is impossible.
2. That coitus is possible only when the vaginal closure is high.
3. That menstrual blood, which must find its exit through the bladder, sometimes causes cystitis.
4. That the contact of urine with the cervix may cause, or lead to, metritis.
5. That sometimes pyelonephritis and vesical calculus result from the stagnation and decomposition of urine in the vaginal pouch.

In spite of these objections, however, Pozzi and most German and English gynaecologists consider the operation warrantable in cases otherwise inoperable. In this country colpocleisis has been regarded with some disfavor. Notably, Emmet condemns it, declaring that it is better for the patient to dribble urine over her person all her life than to submit to closure of the vagina. [1] Hirst, in a recent paper, reports two cases of colpocleisis, and gives his approval of the pro-

[1] American Journal of Obstetrics, February, 1896.

cedure, when the choice must lie between vaginal closure and permanent vesical incontinence.

Regarding the several objections to the operation, it would seem that the wishes of the patient and her husband would be the chief criterion in deciding on the course to be pursued: if they prefer sterility and more or less imperfect coitus to years of misery and discomfort on the part of the woman, surely the first two objections above stated disappear. In young women, vaginal closure would be resorted to, naturally, with more hesitation than in those near the menopause. It cannot be denied that retention of urine and and menstrual blood in a vaginal pouch above the point of closure may lead to metritis, cystitis and perhaps to calculus and surgical kidney, if the case receives neither supervision nor treatment. But menstrual blood in the bladder does not necessarily cause any ill effects, certainly none that cannot be overcome by occasional irrigation; and if, as in the writer's case, the posterior denudation is carried high on the posterior vaginal wall, so that the septum is sharply beveled towards the bladder, there is no considerable vaginal pouch to contain residual urine or menstrual blood. Hirst, in his paper above quoted, says that it has been his experience, that in many cases of bad, neglected fistulae, surgical kidney exists in consequence of the fistula. The writer can well accept this statement from his observation of the case reported. It was observed that, as the patient lay in bed before operation, the sphincteric action of the vaginal introitus was such that considerable amounts of urine were retained in the vagina, which thus became a supplementary bladder: this urine was retained until active movement of the patient or digital depression of the perineum released it, or until the vagina was considerably distended.

The writer regrets that all efforts to trace the case reported since she left the hospital have been fruitless; it is only known that she has left this vicinity. The present condition of the patient cannot, therefore, be stated; but from his study of this case and of the literature of the subject the writer has arrived at the opinion that colpocleisis is a legitimate operation in cases otherwise inoperable, when accepted by the patient and her husband with a full knowledge of its

consequences; that in the performance of the operation it is important to close the vagina as high as possible, and to bevel the septum sharply towards the bladder; that it is desirable to keep the patient under occasional observation after operation, with a view to the prevention or early removal of any difficulty that may possibly arise from menstrual blood or residual urine in the bladder or vaginal pouch.

XI.

THE LOCAL ANÆSTHETICS USED IN THE EYE.

By Walter B. Lancaster, M.D.

The list of drugs known to produce local anæsthesia is a long and rapidly increasing one, although for some years after Koller, in 1884, showed the practical value of cocaine as a local anæsthetic all attempts to find other drugs with this property were fruitless. O. Bergmeister and E. Ludwig, examined a large number of alkaloids in the hope of finding some succedaneum for cocaine, and perhaps one less costly than cocaine then was. They were unsuccessful.

Apomorphine was shown to be capable of producing local anæsthesia in the eye. It must be used in such large quantities, however, as to produce constitutional effect (vomiting), and for this reason was not available in practice. For a similar reason brucine could not be used. Menthol, carbolic acid and similar drugs are too irritating for use in the eye, though useful as local anæsthetics elsewhere.

Some vain hopes were kindled by Lewin's announcing that erythrophlæine hydrochlorate was an effective and useful anæsthetic. This alkaloid is derived from sassy bark, an ordeal poison of West Africa. It was soon found that erythrophlæine was such a powerful poison that it was not safe for use in the eye in sufficient concentration to be effective.

Erythrophlæine belongs to the group of cardiac poisons of which digitalis is the most important member. It was suggested by Lauder Brunton, that not improbably other members of this group would prove to have anæsthetic properties. Accordingly, C. Rommel[1] examined as many of these as he could obtain, and found that Lauder Brunton's surmise was correct. The glucosides helleborein, convallamarin, strophantin and adonidin and the alkaloids carpaine hydrochlorate

(from flowers of carica Papaya) and Muawinum hydrobromate (ordeal poison from Mozambique) all proved capable of producing diminution of sensibility in conjunctiva and cornea. They were slow in acting, according to Rommel, requiring from one-half an hour to three or four hours before anæsthesia was produced after one instillation, the effect lasting hours and even days. They were all more or less irritating, causing congestion of conjunctival and ciliary vessels and lachrymation, so that even the best could not rival cocaine. Two of them were used for some weeks in his eye clinic, but given up. Six or seven other drugs of this group of heart poisons were examined, but no others showed anæsthetic properties.

There are a number of other drugs which produce local anæsthesia which, so far as I know, have not been tried on the eye. Antipyrine causes prolonged anæsthesia of the mucous membrane of the throat, but must be used in concentration of thirty per cent. to produce the best results (St. Hilaire[2]), and a five per cent. solution causes sharp stinging in my own eye and is too weak to produce anæsthesia. Acetanilide, in saturated aqueous solution (one to two hundred), I found, is also too irritating to use in the eye, though it has anæsthetic properties applied to wounds or mucous membranes, slight because of its slight solubility. Guaiacol was brought forward by Lucas-Championnière[3] as a local anæsthetic for minor operations used hypodermically. It also is, I believe, too irritating for use in the eye.

Meantime the chemists were searching along two lines: First, in the leaves of Erythroxylon coca and allied species, for alkaloids of similar properties to cocaine; second, by a thorough study of the chemical constitution and relations of cocaine to make synthetically compounds of similar properties. As a result of the search in nature for other alkaloids like cocaine, a considerable number were found in coca leaves of various species, but only one promised to be of practical value, viz., tropacocaine. This was found by Giesel in leaves of a small-leaved coca plant of Java. It was also made synthetically.

Chadbourne[4] made a study of tropacocaine pharmacologically. His conclusions were that, as compared with cocaine,

it was less than half as toxic and less uncertain in its toxicity. On the eye, that anæsthesia was more rapidly induced (one minute and forty seconds *vs.* two minutes and three seconds for cocaine) that a weaker solution was effective, that it was less irritating, kept far better and had very little effect on the pupil. From my own experience with tropacocaine, I should say that it was less effective than cocaine instead of more, and I think that is the general verdict. Doubtless the variation in different samples of the drug makes a difference in the results as has been pointed out by Chadbourne. Although it is now some years since it was introduced, tropacocaine has not won an important place in practice, chiefly I think on account of its high cost. If a uniform and less expensive preparation were put upon the market it would come into more general use for the purposes of a mild and safe anæsthetic.

On the chemistry of cocaine much work has been done by Einhorn, Liebreich, Ehrlich, Poulsson, Filehne and many others. At first the chief practical outcome of this was in improved methods of extracting the drug from the coca leaves and purifying it, and in pointing out that certain impurities caused some of the disagreeable and dangerous symptoms observed after using cocaine. They also explained why cocaine cannot be boiled or kept long without deterioration (decomposition).

In attempting to construct synthetically allied compounds which might have anæsthetic properties, the first step was to ascertain whether any part of the cocaine molecule would retain in itself the anæsthetic property of the whole. To this a negative answer was given. Cocaine is benzoylecgoninmethylester. It was found that neither benzoylecgonin nor ecgoninmethylester, nor ecgonin possessed any anæsthetic properties.

The next step was to try the effects of allied compounds with some group of atoms in common with cocaine. Working along this line Filehne concluded that it was to the benzoyle group (O C O C_6 H_5) that cocaine owed its anæsthetic property, for he found many benzoylated alkaloids had power to produce anæsthesia; for example, benzoyl-tropine, benzoyl-morphine, b.-quinine, b.-cinchonine, b.-hydrocotar-

nine, etc. According to this view cocaine (benzoylecgoninmethylester) owed its anæsthetic property to the benzoyle group, but substituting other acid radicals for the benzoyle radical, it appeared that a few of these had anæsthetic properties, *e.g.*, phenylacetylecgoninmethylester. Hence Ehrlich concluded that the anæsthetic property belonged to those "cocaine bodies" into whose composition there entered certain acid radicals which he called *æsthesiophores*. Of these radicals, benzoyle is the most important.

But there are other ways of splitting up the cocaine molecule besides into benzoylecgoninmethylester. It may be regarded as a double ring (Einhorn), n-methylbenzoyloxypiperidincarbonicacidmethylester and benzoyloxyhexahydrobenzoicacidmethylester, in which the benzoyloxymethylester is common to both. Might not n-methyl-etc., be the factor causing anæsthesia. Merling, working along this line, constructed synthetically n-methylbenzoyltetramethyloxypiperidincarbonicacidmethylester, which is called *eucaine* A for short. The hydrochlorate of this compound is a soluble crystalline salt. Its action when administered to animals is similar to that of cocaine, though less toxic. Locally, it produces, like cocaine, loss of sensation, but, unlike cocaine does not stimulate the sympathetic nerve, so that it does not dilate the pupil, or does so very slightly, and causes hyperæmia instead of ischæmia. I experimented with a sample sent me by the New York agents of the manufacturers and found it decidedly more irritating than cocaine, and that is the verdict of the majority of observers. The manufacturers do not now recommend its use in the eye.

The other half of the double ring — the hydrated benzoyloxybenzoicacidmethylester — was studied also, and Einhorn and Heinz[5] are still working on the derivatives of this group. They found that some of the series formed salts with anæsthetic properties, and were led to try whether, as in the case of cocaine, the simpler substances into which these split lost the anæsthetic property. To their surprise they found the simple ester was more active as local anaesthetic than the benzoylated compound. This observation led to the examination of the whole series, by which it was shown that all the aromatic amido oxyacids form local

anæsthetics varying much in degree, but in no case without anæsthetic power. Other related esters were tried, and Einhorn and Heinz give a partial list of them, numbering about forty, all of which have more or less anæsthetic power, and some of which may prove useful in practice.

In particular, they speak very favorably of p. amido-m. oxybenzoicacidmethylester, called *orthoform* for short. I obtained a specimen of this through the courtesy of Professor Einhorn, but too late for detailed report here. It is not a substitute for cocaine, but has a distinctly different field of usefulness. It is very slowly soluble, and therefore its action is prolonged. It is non-toxic, and therefore may be used freely. The chief indication for its use is pain in any part where the drug can be brought in contact with the painful nerve ending; therefore not deep-seated pain but superficial, as in ulcers, burns, where the skin is destroyed (because it does not act through the skin), ulcerating neoplasms, granulating surfaces. It is said to be antiseptic and to diminish secretion, and therefore to be of value as an application to wounds.

As far as I have tried orthoform, my experience corroborates the above. Introduced into the eye as a powder, or ten per cent. salve, it causes at first no special sensation, because slowly soluble, but after a minute or two some burning and smarting, which passes off soon, and is followed by diminished sensibility to pain. Tactile and temperature sensibility are not much if at all affected. It will probably fail to produce such prolonged action (one to several days) when used in the eye as when used where there is no such constant flow of liquid to wash away the drug. Its chief field will probably be elsewhere. Another reason for this is that the amount of irritation caused in the eye is sometimes considerable.

Vámossy,[6] of Budapesth, has lately set forth the claims of another drug as a local anæsthetic, an old one in new form. Acetone chloroform was introduced by Willgerodt. In physiological action it is an hypnotic. That it is a local anæsthetic was pointed out by Kossa, but since it is insoluble in water it was not thought to be available for practical use for that purpose. Vámossy has succeeded in obtaining a one to

two per cent. aqueous solution which he calls *anesin*. This acts as a local anæsthetic if applied very freely. Used like cocaine it has little effect, but by bathing the eye in the solution by steady continuous dropping for a minute, superficial anæsthesia is obtained. It has, he says, no irritant action and no effect on the pupil. It has been used hypodermically with alleged brilliant results as a local anæsthetic. I have not had an opportunity to try anesin but my impression is that the solution will not prove of any practical use in the eye.

None of the drugs so far named has proved a serious rival of cocaine. There are two others, however, which, from the published reports, would appear to have better claims for notice — eucaine B and holocaine.

Eucaine B is allied chemically to eucaine A, as its name implies, and therefore to cocaine and especially to tropacocaine. It was introduced to take the place of eucaine A for use in the eye, as that was found to be too irritating for the eye and is recommended for use elsewhere only, *e.g.*, throat and hypodermically. The chemical name of eucaine B is benzoylvinyldiacetonalkamine. It was discovered by Merling. The hydrochlorate forms white crystals soluble to three or three and one-half per cent. in water at ordinary temperature. It is not injured by boiling. In physiological action it resembles eucaine A and cocaine, but is less poisonous than either. Its local action is apparently the same as that of eucaine A, except that it is less irritating.

Holocaine was introduced by Täuber. It is *p. diaethoxyaethenyldiphenylamidin*. It therefore belongs to the amidin group and is not allied to cocaine. It is made from phenacetin and Täuber was led to its discovery by the fact that other allied compounds had proved useful — phenacetin and lactophenin. Holocaine is a powerful base and forms crystalline salts. The hydrochlorate is soluble in hot and, with difficulty, in cold water. The solution is neutral and permanent. It is not affected by heat but is decomposed by even a minute trace of alkali into H Cl and holocaine which, being insoluble, forms a precipitate and is the cause of a turbidity seen when the solution is boiled in ordinary glass because of the faint trace of alkali which is dissolved out of the glass by boiling water. The physiological action of holocaine when ab-

sorbed is that of a convulsant poison, like strychnine, also resembling curare in some respects. It is about five times as poisonous as cocaine (Heinz). It is an antiseptic of considerable strength, a one per cent. solution completely stops putrefaction and fermentation and even kills vegetating bacteria (Heinz and Schlosser[7]). Local action: a few drops of one per cent. solution dropped in the eye causes moderate irritation, lasting about three-fourths of a minute, and followed by diminished sensibility. The congestion is usually slight but persists for some minutes. There is no effect on the pupil except from the irritation. The local action of holocaine is much the same as of eucaine B, except that it is more irritating.

A large number of articles have appeared giving the experience of the writers with eucaine B or with holocaine and nearly all of these reports have been favorable. My observations cover a little over six months. The specimens of the drugs which I used were obtained of different local druggists and also from the German manufacturers direct (holocaine) and from the New York agents (eucaine A and B). My object was to compare the local action on the eye of these drugs with that of cocaine, to aid in determining their relative merits and fields of usefulness. The method of experimenting was, in the case of normal eyes (and of inflamed eyes when both were about alike) to introduce two drops of one solution in one eye and an equal quantity of the solution to be compared in the opposite eye. When the test was made on inflamed eyes one drug was used after the other at a sufficient interval to allow the effect of the first to pass off. To test the sensation I used a wisp of cotton, a blunt probe and a pair of forceps, the last to pinch the conjunctiva. I selected when possible more intelligent patients and tried to avoid leading questions.

I first made a number of trials of cocaine, as the published reports of its action are somewhat contradictory. The effects produced by the instillation of a cocaine solution into the eye are at first those of irritation, such as follow any other slight irritant, viz., slight smarting and burning with congestion, lachrymation, reflex blepharospasm and possibly slight alteration of the pupil. These are soon followed by the

specific effects of cocaine on the nerves, viz., paralysis of the sensory and stimulation of the sympathetic. The first (paralysis of the sensory) causes anæsthesia of the cornea and conjunctiva, diminished reflexes, especially winking, and if a sufficient quantity is used some anæsthesia of the deeper tissues, subconjunctival and intraocular. The second (stimulation of the sympathetic) causes contraction of those unstriped muscular fibres of the eye, which are innervated by the sympathetic, viz., the vaso-motor fibres, dilator of the iris and Müller's muscle. The vaso-motor contraction causes ischæmia and so follow, sense of coolness, diminished secretion (due in part to diminished reflex) and diminished intraocular tension. The contraction of the dilator of the iris (aided by vaso-motor contraction of the vessels of iris) causes dilatation of the pupil; as the sphincter muscle of the iris is not affected, being innervated by the third nerve, the pupil reacts to light and contracts during sleep. The contraction of Müller's muscles produces retraction of the eyelids and increased prominence of the eyeballs. If a considerable amount of cocaine is used, and particularly of a strong solution, and it is much more marked if the eye is not kept shut and protected from the air, as may readily happen because of the diminished reflex winking, a peculiar change takes place in the cornea. It seems to become drier ("lymphanæmia") and the epithelium becomes rough and loses its transparency, and may peel off in part. Hence the cornea has more absorptive power, as shown by the way fluorescein or other dye penetrates the tissue. It is claimed by Mellinger[8] that the cornea also loses in elasticity, and hence more readily collapses when cut, as for cataract extraction, and that the anterior chamber is more slowly restored. He further states that the primary coaptation of such wounds is less perfect, and firm union longer delayed than when cocaine is not used. Finally, in some cases, toxic systemic effects are produced. A tendency to collapse is the most important of these, cocaine being a cardiac poison. It is important to note that the symptoms of cocaine poisoning are so like those of shock that probably many cases of simple nervous shock causing syncope have been attributed to the toxic action of cocaine. There seem to be well authenticated

cases, however, where a very small amount of cocaine used in the eye produced severe symptoms. Of course, after freely using strong solutions, such symptoms are less rare.

I found some apparent contradiction in the published statements about the time required to produce anæsthesia after the instillation of cocaine. The average time given is five to ten minutes; the extremes being ten to twenty minutes (Noyes' text-book) and a few seconds (Mittendorf, Hare's Syst. Therap.). To determine this point I made many trials and with uniform results. The instillation of two drops of a two per cent. solution of cocaine hydrochlorate in normal eyes produces anæsthesia of the cornea in forty to sixty seconds, when tested by a wisp of cotton. If tested by a blunt probe a gentle touch is not felt as pain but is usually felt as a sensation of touch or temperature. If the conjunctiva is pinched by a pair of forceps it is felt as pain, though much less than in the opposite eye where no cocaine has been used. In other words, there is a diminution but not an abolition of sensation, more marked and rapid of cornea than of conjunctiva, and of pain more than of touch or temperature. The degree of anæsthesia increases somewhat during the following minutes, but some sensation still remains. It is difficult to say when the maximum is first reached, because the increase is so gradual and slight after the first minute, but it is within three to five minutes. By repeating the instillation at intervals of two or three minutes, the diminution of sensibility is so great after eight or ten minutes that only by careful attention can the subject tell when the conjunctiva is pinched or the cornea pressed upon or scratched, and then probably by the transmission of the pull or pressure to the deeper tissues, which can hardly be avoided. The time when the smarting of the first instillation ceases is a good guide to when a fair degree of anæsthesia is obtained. The fact that the second or subsequent instillation causes smarting is proof that the anæsthesia is not complete.

The most important disadvantages charged to cocaine are: toxicity, injurious effect on the cornea, mydriatic effect and consequent danger of inducing an attack of glaucoma. These are serious drawbacks but it is easy to exaggerate them and it is not difficult to avoid them in the vast majority of cases.

To avoid the poisoning it is only necessary to confine one-self to two, or for occasional use, four per cent. solutions, and to use no larger quantity than is necessary — two or three drops, two or three times repeated need rarely be exceeded, *i.e.*, cases which resist this amount will hardly be made anæsthetic by more.

To avoid injuring the cornea it is only necessary, in addition to observing the above precautions about strength and quantity of solution, to keep the eye shut and protected from air during operations. While the eye must be kept open, occasional moistening of the cornea by salt solution or boric acid solution, or whatever solution of the kind is preferred by the operator, will be sufficient protection.

The mydriatic property of cocaine is, to my mind, a very valuable one, and far from a disadvantage. It is the least objectionable agent we have to dilate the pupil for ophthalmoscopic examination. If one fears to cause glaucoma by using it as an anæsthetic, it is easy to overcome the weak mydriatic effect of cocaine by the stronger myotic action of pilocarpine or eserine, either in combination with cocaine in the same solution, or used before or immediately after. On the other hand, the power which cocaine has of reducing intraocular tension makes it a valuable aid to relieve the high tension of glaucoma, when combined with a myotic, whose action it reinforces. This power to reduce tension can be used to advantage in cases where intraocular hemorrhage is feared. The less the intraocular tension before operation, the less strain is put on the blood vessels when the intraocular tension is more or less suddenly reduced to zero by escape of the aqueous when the anterior chamber is opened. Therefore, in case intraocular hemorrhage is feared, the indications seem to be to keep the general blood tension as low as possible; to use cocaine longer and more freely than usual before operation, in order to reduce if possible the intraocular tension; and to be careful to allow the aqueous to escape slowly and gradually. Some operators complain of the reduction in intraocular tension as interfering with the performance of cataract operations, because it is harder to make a good cut of the cornea when the eye is soft, but if care is taken not to have cocaine instilled until five minutes

or less, before the operation, the reduction of tension will not usually have begun to show itself.

The local action of eucaine B and of holocaine differs from that of cocaine chiefly in that they do not stimulate the sympathetic, and so cause dilatation of pupil and ischæmia and its consequences. They also have less effect on the cornea when the eye is exposed to the air. It is important to note that eucaine B is used in three per cent. solution and holocaine in one per cent., or less, and that the bad results from cocaine are rarely seen from such weak solutions. The relative insolubility of eucaine B and holocaine is therefore a safeguard against strong solutions, though curtailing their adaptability to varied uses. The initial irritation following the instillation of eucaine B and holocaine is more marked than with cocaine, and the hyperæmia does not give way to ischæmia but continues with only slight diminution for some time. Patients almost without exception find the smarting more disagreeable with eucaine B, and considerably more with holocaine, than with cocaine. I remember but one patient who said the eye in which I put eucaine B smarted less than the opposite eye in which I put cocaine. All other cases with eucaine B and holocaine said the cocaine was less disagreeable, except a few who detected no difference. Perhaps that single case was due to a fault in manipulation by which I did not get equal amounts in each eye.

What then are the advantages of eucaine B as compared with cocaine?

1. It is less toxic. In most cases this is of little moment; in a case known or feared to be susceptible to cocaine it would be of considerable importance.

2. It can be sterilized by boiling. This is a decided advantage. Many surgeons combine an antiseptic with their cocaine solution. This does not render it surely sterile and increases the irritation caused by the solution. Many cases of opacity of the cornea, some of them permanent, have been attributed to the combined effect of cocaine and corrosive sublimate used in operations on the eye, though other surgeons have used them for years freely together without seeing bad results. It seems to me that the best way is to prepare the cocaine solution freshly in sterile salt solution or sterile water.

It is in this way that the cocaine used in these experiments for comparison to eucaine, etc., was made except in a few cases. A sample solution so prepared was found by Dr. R. M. Pearce to be sterile. If a large number were examined doubtless some would be found to contain bacteria, more frequently non-pathogenic than pathogenic.

3. It can be used without a myotic when it is feared that dilatation of the pupil would be dangerous.

4. It does not injure the cornea, at least no cases of such injury have yet been reported.

5. The solution keeps fairly well.

What are the disadvantages of eucaine B?

It is slightly more irritating and less effective than cocaine. Hemorrhage is likely to be freer.

What are the advantages of holocaine?

1. It is antiseptic and its solutions do not need to be boiled (Heinz), (though they can be, with care to avoid alkalis) and they keep very well. My experience, as far as it goes, corroborates this. Dr. Pearce examined a solution I had been using for four months, not including a month's vacation, and, except for a mould (which grew on the cork during vacation) he found no organisms in the solution. This is certainly a decided advantage.

2. It is claimed that anæsthesia is much more rapidly produced with holocaine. That is because the time for cocaine is set too high. The time usually stated for holocaine is three-fourths to one minute. That is what I found, and it is also what I found for cocaine, so that in this respect there is no advantage either way.

3. It is claimed for holocaine that it acts on inflamed eyes, and therefore is superior to cocaine. I made a number of trials of this point, and found that it was not possible to produce anæsthesia in inflamed eyes with holocaine any more than with cocaine. It is possible to diminish sensibility considerably, but fully as much — I think more — with cocaine than with holocaine. Foreign bodies were removed in many cases with the aid of holocaine, and also eucaine B, but the general impression I obtained was that cocaine worked better than either. Besides, in an eye already irritated, it seems

more reasonable to use an agent which reduces congestion than one which increases it.

Example: H. Foreign body (emery) cornea, over a month considerable congestion, cloudiness in cornea about foreign body. Holocaine three times — not anæsthetic.

G. Wooden splinter obliquely buried in superficial layer of cornea, considerable congestion. Holocaine three times, — not anæsthetic.

Similar results were obtained with eucaine B, except rather less irritation than with holocaine and perhaps less diminution in sensibility.

J. M'R. Foreign body in cornea, cocaine four times, — not anæsthetic. Waited half an hour, holocaine twice at one minute interval, followed by pain (which increased, and after three minutes diminished) and by congestion, lachrymation and photophobia; after five minutes, holocaine two drops, which smarted severely. If any effect of the cocaine was left in this case after half an hour it would so far help the holocaine; yet in this, and every other case, the holocaine caused more pain, and the second and subsequent instillations also caused pain, showing that the eye was not anæsthetic. The patients invariably preferred cocaine.

C. F. Foreign body, cornea, since five to six weeks, been treated with atropine, slight ciliary injection. Cocaine used five times cornea not anæsthetic (though sensibility sufficiently diminished for removal of foreign body), ciliary congestion disappeared, conjunctiva blanched. Later, holocaine four times; much more smarting than with cocaine and moderate general congestion.

From these and numerous similar cases I am convinced that holocaine can not produce more, if as much, anæsthesia in inflamed and irritated eyes as cocaine.

4. Like eucaine B it can be used without a myotic in cases where it is feared that dilatation of the pupil might cause an attack of glaucoma.

5. It is claimed that holocaine does not injure the cornea. Some injurious effect on the cornea in rabbits has been observed by Heinz & Schlosser. A case of severe damage to cornea and conjunctiva in a human eye has been reported recently by Emil Bock.[9] Five grammes of a one per cent. solution were used by repeated instillation, most of the solution ran out of the eye. The conjunctiva became red, swollen, stiff, opaque, with folds of light gray color; cornea rough and smoky, surrounded by a narrow, dense, gray, marginal opac-

ity. The eye cleared up after ten days. It appears that holocaine is not devoid of power to do harm to cornea and conjunctiva.

The disadvantages of holocaine are its extreme sensitiveness to alkalis; its more irritating action; the congestion and tendency to more annoying hemorrhage; its great toxicity.

It is evident that cocaine has a much wider field of usefulness than its rivals, owing to its acting not only on the sensory nerves but on the sympathetic. In those cases where it is desired to avoid this, and yet not desired to use pilocarpine or eserine, eucaine B or holocaine may be chosen. As between these two I prefer eucaine B as less irritating and less toxic, and less easily decomposed, though holocaine is perhaps more active as an anæsthetic, and is superior in being antiseptic. I prefer to use the least irritating solutions possible, and in this respect two per cent. cocaine, freshly prepared in sterile, one per cent. salt solution (the strength of tears) or in normal salt solution, is decidedly superior to any. In keeping qualities and ease of sterilization, solutions of eucaine B and holocaine both, are superior to cocaine solutions, and that is the only decided advantage I have found, unless we add cheapness.

I desire to thank Dr. Folsom for permission to test the anæsthetics on convalescent patients of the first medical service, and Dr. Pearce for making bacteriological examinations.

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XII.

FORMALDEHYDE AS A PRACTICAL DISINFECTANT AND AS AN AID IN THE PRACTICE OF SURGERY.[1]

CHARLES HARRINGTON, M.D. AND RICHARD MILLS PEARCE, M.D.

FORMALDEHYDE as a practical disinfectant has been the subject of much investigation during the past two years, particularly with reference to the best means of producing it directly from methyl alcohol or of liberating it from its forty per cent. solution in water ("Formalin"), and to its action on exposed and protected organisms. Among the results of this work have been the invention of a considerable number of lamps and autoclaves, and much conflicting evidence as to its germicidal power. Lately, Aronson demonstrated the value of the polymerized formaldehyde, the solid paraformaldehyde, which can be volatilized in lamps of very simple construction and without danger of fire or explosion.

In September last, we undertook a series of experiments to determine the germicidal power of the agent in solution and in its polymerized form, its practicability as a room disinfectant, its penetrating power, its usefulness as a disinfectant for surgical instruments and sutures, and its action on higher organisms.

The organisms regularly employed were the staphylococcus pyogenes aureus, the typhoid bacillus, anthrax spores and a non-pathogenic spore bearing bacillus of high resistance. Others were occasionally employed as will be noted. All cultures used, excepting those of the spore-bearers, were from twenty-four to forty-eight hours old, and were made on blood-serum or bouillon; those of the spore-bearers were from four to ten days old. All tests were made on blood-

[1] The experiments on which this paper is based have been reported for the most part in an article in the American Journal of Medical Sciences, "The Possibilities and Limitations of Formaldehyde as a General Disinfectant."

serum or bouillon, and all reported as negative were so at the end of seventy-two hours.

The first experiment was made in the Bacteriological Laboratory of the hospital, a room 26.75 feet long, 19.75 feet wide and 14.50 high, thus having a capacity of 7,660.5 cubic feet.

The tests employed were as follows: On one of the two large desks, which we will call Desk A, 250 cc. of typhoid infected milk in a quart pitcher; biscuit smeared with typhoid (bouillon culture) and tied up in a napkin; anthrax spores inside a small pear; smears of anthrax spores, typhoid and non-pathogenic spore-bearer on paper (exposed); same and one of diphtheria (throat culture) in thin blank-books; smear of staphylococcus aureus inside thin blank-book near binding (the book tightly closed); two rabbits in a wire cage, one with anthrax spores, the other with non-pathogenic spore-bearer smeared on the head.

On the other desk, which we will call Desk B: Typhoid infected sheet and blanket, tied up in a clean sheet; typhoid stool in a basin covered with a towel; two dressings (twenty-fours hours old) from an empyema; dressing (seventeen hours old) from an abdominal wound; dressing from fecal fistula (corrosive and iodol; on three hours); one uncovered and five covered Petri dishes containing water with an abundance of water bacteria; two uncovered Petri dishes containing respectively pond water and sour milk in thin layers; racks containing cotton-stoppered test-tubes of bouillon and serum cultures of the typhoid and diphtheria bacilli, staphylococcus albus and aureus, and non-pathogenic spore-bearer.

In Thermostat: Cotton-stoppered tubes of diphtheria bacilli and anthrax spores, and exposed smears of the same on paper.

In covered galvanized iron barrel eight feet to the side of the door: Lot of surgical dressings, including one from a septic compound fracture of the tibia, wrapped in paper and cotton.

In order to have other than bacteriological tests of the diffusion of the gas, thirty-three Erlenmeyer flasks containing decolorized fuchsin solution and stoppered with absorb-

ent cotton, were placed in various parts of the room; on several of the shelves in different parts of the room, at the top of the lower sash of each window, in and on the dry sterilizer fixed to the end wall, in the slop-jars under the desks at the windows, in closed cupboards under desk B, in five closed drawers in desk B, on desk B next to the typhoid stool, on and near the rabbit cage, next to pitcher and pear on desk A, in the slop-jar under the sink, in and on the thermostat, in an open tin box next to the hood and six feet from the floor, in the barrel, and in the lower drawer of the end desk by the windows. A control flask was placed in another room. This solution, made by passing a stream of sulphurous acid gas through a dilute solution of fuchsin (1:1,000) until the color is discharged, had been found to be extremely sensitive to the presence of formaldehyde gas in the air, even when contained in flasks, plugged with cotton as in bacteriological work. A very small trace of formaldehyde in the air is sufficient to more or less completely restore the original color.

The room was closed, the crack under the door stopped with wet cotton, and the gas introduced through a fine tube which passed through the key-hole. The apparatus used was the lamp manufactured by the Sanitary Construction Company in which the formalin is slowly admitted to a heated spiral tube and vaporized. In the tank of the apparatus, at the beginning of the experiment, was 2,400 cc. formalin. The lamp worked badly, and finally, owing to persistent clogging of the tube, its use was abandoned until the next morning. Only 650 cc. of formalin had been consumed. On the following morning, after an interval of fifteen hours, the room was opened and aired. Ten cultures were taken at random from as many test-objects and all but two of them yielded good growths.

Examination of the Erlenmeyer flasks showed slight restoration of color in the contents of those on the six shelves between the windows, in the slop-jar, on the shelves over the sink, in the thermostat, on desk B near typhoid stool, on desk A near the milk pitcher, in the barrel over the middle window, and in two of the drawers of desk B. In the flask on the thermostat in the hood, which was near the outlet

flue, the register of which was closed, but not hermetically, the color of the solution had been almost completely restored. The fluid in all the other flasks was unchanged in appearance. The rabbits, which soon after the beginning of the experiment had shown signs of discomfort, appeared to be not much affected.

The room was again closed as before, and the lamp, which had been put in order, was again applied and the experiment resumed. The tank contained 2,550 cc. formalin, and when the apparatus was removed, 2,150 cc. had been consumed. On the following morning, after the same exposure as before, the room was opened and quickly aired. On entering the room, the atmosphere was almost unbearably irritating to the eyes and nose. Contrary to what was to have been expected from the articles by Pfuhl, Aronson, Rosenberg and others, one of the rabbits was dead, and the other was breathing through the mouth with great difficulty. This one improved noticeably within the next two hours, but died thirty-six hours later.

Examination of the flasks containing decolorized fuchsin solution showed that with one exception the color of the liquid had been more or less completely restored. Those showing the greatest intensity of action were on the six shelves between the windows, at the tops of the lower sashes, in and on the thermostat, and in the tin box next to the hood. In these cases the color was completely restored. Those showing the least action were in the drawers and cupboards; their color was light amethyst. The remaining flasks, wherever placed, showed a color of greater or less depth between these extremes.

The one flask showing no change was on desk A, and examination showed that its stopper was much more tightly compressed than any of the others. The control flask was unchanged. Cultures were made from the following:

Smear of anthrax spores on desk A.
Smear of typhoid bacilli on desk A.
Smear of non-path. spore-bearer on desk A.
Smear of diphtheria bacilli in blank-book.
Smear of typhoid in blank-book.

Smear of anthrax spores in blank-book.
Smear of non-path. spore-bearer in blank-book.
Biscuit (typhoid smear) in napkin.
Uncovered Petri dish of water.
Uncovered Petri dish of pond water.
Uncovered Petri dish of sour milk.
Water standing in the sink (shallow).
Dust in crack of floor farthest from door.
Dust in crack of floor near door.
Dust on lowest shelf between windows.
Dust in cupboard of desk B.
Dust in drawers of desk B.
Fluid on bottom of refuse pail.
Material on bottom of slop-jar No. 3 (dry).
Fecal fistula dressing on desk B.
Anthrax spores in hair of rabbit.
Non-path. spore-bearer in hair of rabbit.
Dried feces of rabbit.
Mouth of live rabbit.
Nares of dead rabbit.
Tongue of dead rabbit.
Lung of dead rabbit.

From none of the above was there any growth in seventy-two hours. Cultures from the following showed growth:

Dressing from empyema on desk B.
Dressing from abdominal wound on desk B.
Dressing from septic fracture in barrel.
Typhoid sheet and blanket tied in clean sheet.
Typhoid feces in basin covered with towel.
Closed tubes of anthrax spores and diphtheria bacilli in thermostat.
Paper smears of anthrax spores and diphtheria bacilli in thermostat.
Typhoid infected milk in pitcher.
Pear containing anthrax spores.
Smear of staphylococcus aureus in tightly closed book.
Closed typhoid bouillon tubes.
Closed tubes of staphylococcus aureus and albus, and diphtheria.

Closed tube of typhoid bacilli on blood-serum.
Slop-jar No. 1 containing water.
Slop-jar No. 2, dry (non-path, spore-bearer).
Galvanized iron barrel (covered).
Covered Petri dishes.
Dust on top shelf (spores).
Nares of live rabbit (spores).
Small intestine of rabbit.
Large intestine of rabbit.
Stomach of rabbit (three colonies of a spore-bearing bacillus).

Autopsy of the rabbit which was found dead showed great hyperaemia and increased moisture of the respiratory passages and congestion of the lungs.

The other rabbit was found dead thirty-six hours later. The autopsy showed the same conditions of the respiratory passages and an irregular solidification of about two-thirds of the right lung and about one-half of the left, with increase of fluid in the pleural cavity. Cultures from the solidified portions of the lungs yielded no growth.

Further examination showed the following conditions:

No. 1. Section of the tongue shows nothing abnormal. Section of mucous membrane of the mouth shows desquamation of the surface epithelium with hemorrhage and infiltration, with lymphoid cells in the tissue beneath. Section of oesophagus is normal. There is no pneumonia. The liver shows marked injection, with granular and fatty degeneration of cells around the central veins of lobules. The lymphatic gland shows some dilatation of the lymph sinuses with hemorrhage. In the kidney there is slight degeneration of the epithelium.

No. 2. In the liver there is considerable dilatation of hepatic veins, with some degeneration of liver cells in the centre of the lobules. The kidney is congested. The epithelium of the convoluted tubules is somewhat swollen and granular, and there is a small amount of coagulated albumin in the capsular space of the glomeruli. In many of the convoluted tubules there is more or less granular and circular reticulum, and, in places, desquamation of the cells. The

spleen shows a slight amount of hemorrhage in the pulp. Pancreas shows no change. One of the lymphatic glands shows a marked degree of oedema, with formation of fibrin in the lymph sinuses. In the lung there is intense bronchitis with consolidation extending into the surrounding lung tissue. This is more marked in the very smallest bronchi. In one place, in the centre of a focus, there are numbers of short bacilli. The exudation of the alveoli is almost entirely purulent, with some large cells mixed with pus. In another place in the tissue there were numbers of large bacilli. There is only a slight amount of fibrin in the exudation. In another portion of the lung there are very much larger foci which are filled with organisms. All the blood vessels of the lung are greatly injected.

It is difficult to explain the absence of bacteria in the cultures made from the lung in the second case. The general character of the lesions in both cases shows the action of a soluble chemical poison on the tissues. The changes are much more marked in the second case than in the first, but in both they are of the same general character.

The next experiment was conducted in the Histological Laboratory, a room 33 feet long, 20.5 wide, and 14.5 high, thus having a capacity of 10,765 cubic feet. Ventilation is provided for by four outlets closed by registers, two of which are two feet two inches by one foot ten inches, the other two just half as large. Two desks similar in size to those in the room in which the first experiment was conducted stand on the floor in similar positions. Experiments on a small scale with flasks and test-tubes having demonstrated that formalin diluted with water can be evaporated by direct application of heat without polymerization, it was determined to try this simple means on a larger scale with the idea that it would be possible to do away with the use of expensive apparatus. The test objects used were as follows:

Smears of anthrax spores, diphtheria bacilli, and non-path. spore-bearer on paper placed on desks, smears of anthrax spores and staphylococcus aureus in desk drawer, closed tubes of diphtheria bacilli and anthrax spores, and open tubes of staphylococcus aureus, anthrax and non-path. spore-bearer, surgical dressings wrapped in paper and

in cotton on the desks, surgical dressings in a cup-board, and a blanket on which was part of a typhoid stool in another cupboard. A glass dish, covered with wire gauze and containing a number of cockroaches, was placed on one of the desks.

Four thousand two hundred and fifty cc. of formalin was mixed with 3,000 cc. of water and placed in a copper cylinder of ten liters capacity, provided with a glass gauge to show the height of the fluid in the cylinder. Heat was applied by means of a small gas-stove, the regulation of which was provided for by having a loop of the rubber supply-tube passed under the door into the hall. The registers were closed, the gas turned on and ignited, the doors closed, and the spaces beneath stopped with wet cotton. In four hours the gas was shut off, and the room was left unopened seventeen hours. On entering the room, it was evident that considerable natural ventilation had occurred, for the discomfort occasioned was but slight in comparison to that noted in the previous experiment. This result had, however, been foreshadowed by the readings of a wet and dry bulb hygrometer which had been placed near enough to the transom to admit of ready observation. At intervals of a half hour the readings were taken, and in spite of the volume of liquid that had been evaporated there had been at no time any marked increase in the degree of moisture in the air. The copper cylinder was found to contain 1,200 cc. of liquid, which contained a large amount of polymerized formaldehyde. Of the test objects employed, only two, the smears of diphtheria bacilli and non-path. spore-bearer were found to have been sterilized.

The next experiment was conducted in Research Room No. 1, a small room of 1,500 cubic feet capacity. In this a Schering lamp was employed with pastilles of polymerized formaldehyde. According to Aronson the proper number of pastilles to be consumed would have been eighty-five, but, as a preliminary test, only twenty were employed, and the results showed that that number was insufficient. The test objects employed were smears of typhoid bacilli, staphylococcus pyogenes aureus, anthrax spores, and non-path. spore-bearer on paper, four surgical dressings, and a smear of diplococcus

intracellularis meningitidis. After eighteen hours' exposure, all but the last-mentioned showed abundant growths.

The next experiment was conducted in one of the surgical operating rooms of 4,560 cubic feet capacity (19 by 15 by 16). The Schering lamp was again tried, this time with half the number of pastilles recommended, that is with 130. Before the lamp, filled with 250 cc. of alcohol, was lighted, cultures of dust were taken in bouillon as follows:

1. Bandage closet.
2. Dead fly on window-ledge.
3. Floor near operating table.
4. Floor near window.
5. Top of marble ledge at window.
6. Crack between water-pipe and floor.
7. Reflector of chandelier.
8. Inlet for heated air under window.

A culture was taken also from a surgical dressing.

All gave abundant growths.

Tests objects consisting of smears of anthrax spores, staphylococcus aureus, typhoid bacilli, and non-path. spore-bearer on paper were placed on a table near the centre of the room. The lamp was lighted, and the door closed. The space under the door was stopped with wet cotton, and the keyhole covered with a gummed label. After twenty-one hours, the room was opened, and at first the atmosphere was unbearable. As soon as possible, cultures were taken from the same places as before and from the exposed smears. Dust from the marble ledge and from the bandage-closet, the door of which had been closed, yielded abandant growths, as did also a culture from the dead fly. Dust from the reflector, from the floor near the window and from the inlet for heated air showed slight growth.

Dust from the floor near wall and under the operating table, the dressing in a pail, and the paper smears were sterile.

Two Petri plates, exposed twenty minutes after airing the room, gave the following results:

1. Plate on table at side of room —
   One colony of a short bacillus.

One colony of staphylococcus pyogenes aureus.
Two colonies of staphylococcus pyogenes albus.
Three colonies of a large yellow coccus.

2. Plate on table in corner of room —
One colony of a brown mould.
One colony of a short bacillus.
One colony of large yellow coccus.
One colony of staphylococcus pyogenes albus.

The next experiment was conducted in an exactly similar adjoining room with two Schering lamps, each carrying 130 pastilles. Before the lamps were lighted, three Petri plates were exposed for twenty-five minutes, with the following results:

Plate on sink at side of room —
Forty-three colonies of non-pathogenic organisms.
Thirty-seven colonies of staphylococcus albus.
Four colonies of staphylococcus aureus.
Two colonies of staphylococcus citreus.

Plate on operating-table at centre of room —
Seventy-nine colonies of non-pathogenic organisms.
Six colonies of staphylococcus aureus.
Thirty-nine colonies of staphylococcus albus.

Plate of instrument-table at corner of room —
Twenty-six colonies of non-pathogenic organisms.
Four colonies of staphylococcus aureus.
Twenty-three colonies of staphylococcus albus.

Before the experiment was begun, dust cultures which yielded abundant growths, were taken from the following:

1. Table at side of room.
2. Reflector.
3. Bandage closet.
4. Floor near window.
5. Floor under operating-table.
6. Crack under water-pipe.
7. Floor at corner of room.
8. Inlet for heated air under window.
9. Marble ledge over sink.

Test objects were introduced as follows:

Smears prepared on papers each of which bore anthrax spores, non-path. spore-bearer, staphylococcus aureus, and typhoid bacilli were encased in small bags made of cotton such as is used in the manufacture of flour-bags. This cotton is very heavily sized, and the bags made from it may readily be filled with water which then runs through with marked slowness. On being boiled in water the sizing is removed, and they are then quite pervious. Both forms, boiled and unboiled, were used. After the smears were introduced, the open ends of the bags were twisted and securely tied. Smears in one bag of each kind were placed on a glass shelf at the side of the room, in the inlet for heated air under the window, and on the reflector of the chandelier.

Smears of the same four organisms were placed in Erlenmeyer flasks and distributed as follows: Two were placed inside a hair mattress well into the hair, the openings by which they were introduced being then securely closed. One was placed in the bandage-closet the door of which was closed, and another, plugged with cotton, in the drug closet, the door of which was left open. In addition to the above, a slightly moist dressing and a wet bloody dressing encased in unboiled bags were placed on a table near the window in company with similar dressings in boiled bags. A rack containing stoppered and open serum tubes was also left on a table.

The lamps were lighted and the room closed as before. After twenty hours' exposure, the door was opened, and, as soon as practicable, three Petri plates were exposed twenty-five minutes as before and in the same situations. On one, two colonies of mould developed; the others were quite free from growths.

Dust cultures taken from the same places as before were sterile with the exception of slight growths of moulds, non-pathogenic bacilli, and a few cocci which were obtained from the floor at the corner of the room and in the closed bandage closet. The smears in all the boiled and unboiled bags and the slightly moist dressings in both bags were sterile. The wet, bloody dressings both showed abundant growths. The smears in flasks in the mattress were both sterile as to typhoid and staphylococcus aureus, but not so as to anthrax spores

and the non-path. spore-bearer. The smear in the flask in the closed bandage closet gave growths of all four organisms, while the one in the plugged flask in the open drug closet was sterile as to typhoid and staphylococcus aureus. Flasks containing decolorized fuchsin solution which were placed alongside the test objects and plugged with cotton, all showed evidence of the chemical action of the gas excepting the one in the bandage-closet where nothing was sterilized. The closed serum tubes after exposure were inoculated with diphtheria bacilli and staphylococcus aureus and albus and showed good growths, while the open tubes, similarly planted, showed only slight growths at the level of the water of condensation.

After a lapse of a week, the experiment was repeated in the same room, using the same lamps and the same number of pastilles, but without the introduction of extra test objects. Dust cultures made from the same places as before showed abundant growths, with the exception of the one from the crack under the water-pipe, which gave no results. An additional culture from the drug closet gave negative results. After an exposure of similar length of time, cultures were again taken, and all were sterile excepting that the one from the closed bandage-closet yielded a very slight growth.

During and after the time in which the foregoing experiments were conducted, a series of experiments was carried on in small air-spaces to determine the amount of formaldehyde, and the length of exposure, required for the sterilization of the various organisms which have been employed, and which may be taken as proper representatives of all pathogenic and non-pathogenic bacteria. Two pieces of apparatus were employed; one, a nearly globular glass bell-jar of 7,500 cc. capacity with an opening at the bottom sufficiently large to admit the hand, and capable of being hermetically sealed with a greased ground-glass plate, and with two small openings in the sides, one of which served to connect with a test tube, and the other provided with a valve to allow for expansion; the other, a nearly cubical glass case of 201,500 cc. capacity, provided with a hinged opening at the lower edge of one side two inches in height, and with a small inlet connected by means of a glass tube and perforated rubber stop-

pers with a small glass flask from which the disinfectant was vaporized by means of a lamp. The results obtained with the small apparatus were, as far as the experiments went, in entire agreement with those obtained with the larger, and need not be detailed. In each experiment the formalin was diluted with a small amount of water in order to ensure complete volatilization without polymerization.

Experiments in glass cabinet:

Experiment 1. Test objects: smears of diphtheria bacilli, typhoid bacilli, anthrax spores, non-path. spore-bearer, and staphylococcus pyogenes aureus; two surgical dressings. Amount of formalin used, 10 cc. Exposure, four hours. Results: all smears, and cultures from outside layers of dressings, sterile; cultures from inside layers of dressings not sterile.

Experiment 2. Test objects: smears as before. Amount used, 5 cc. Exposure, four hours. Results, all sterile.

Experiment 3. Test objects: smears as before, excepting diphtheria, and same smears in boiled and unboiled bags. Amount used, 5 cc. Duration, one, two, three and four hours for exposed smears, two and four hours for smears in bags. Results: smears at one, two, three and four hours, all sterile. Smears in bags at two and four hours, all sterile, except that the smears of anthrax in the boiled and unboiled bags withdrawn at the end of four hours yielded respectively one and three colonies. This last result admits of conjecture but not of explanation.

Experiment 4. Test objects as in Experiment 3. Amount used, 4 cc. Duration, fifteen and thirty minutes for exposed smears, two and four hours for smears in bags. Results: smears, after fifteen minutes, typhoid and staphylococcus aureus sterile: after thirty minutes, all sterile except non-path. spore-bearer. Smears in bags, after two and four hours, all sterile.

Experiment 5. Test objects: same as in Experiments 3 and 4. Amount used, 3 cc. Duration, for exposed smears, fifteen, thirty and forty-five minutes; for smears in bags, one and a half and two and a half hours. Results: smears after fifteen minutes, sterile, excepting non-path. spore-bearer;

after thirty and forty-five minutes, all sterile. Smears in bags, after one and a half and two and a half hours, all sterile. A fly which had entered the cabinet during the airing of the same after Experiment 4, was seen in this experiment to drop dead in fifteen minutes. A culture of the fly taken at the end of the experiment gave negative results.

Experiment 6. Test objects as in Experiments 3, 4 and 5. Amount used, 2 cc. Duration for exposed smears, fifteen, thirty, forty-five and sixty minutes ; for smears in bags, one, two and three hours. Results : exposed smears, after fifteen minutes, none sterile; after thirty and forty-five minutes, typhoid sterile; after sixty minutes, all sterile exceptn onpath. spore-bearer. Smears in bags ; boiled and unboiled bags at end of one hour, typhoid sterile. Unboiled bag at end of two hours, typhoid sterile ; boiled bag, typhoid and staphylococcus aureus sterile. Boiled and unboiled bags at end of three hours, all sterile, except non-path. spore-bearer.

Experiment 7. Test objects, smears on paper (none in bags). Amount used, 1 cc. Exposure, two and a half and four and a half hours. Results: all sterile after both exposures.

Experiment 8. Test objects, as in Experiment 7. Amount used, ½cc. Exposure, two and a half and four and a half hours. Results: all sterile at both exposures. In this experiment, as in Experiment 5, a fly which had entered the cabinet during the airing process was found dead, but how long it survived was not noted.

Experiment 9. This experiment was conducted with the object to determine whether or not it is possible to sterilize surgical dressings and liquid stools by means of any amount of formaldehyde which could be used practically on a large scale. A wet dressing and a liquid typhoid stool in a shallow pan were exposed to an amount of formaldehyde corresponding to one part of liquid formalin vaporized in 5,000 volumes of air, that is to 40 cc. of formalin vaporized in a little over 200,000 volumes of air. Controls taken beforehand showed abundant growths. After eighteen hours' exposure, the typhoid stool was sterile, as were cultures from the upper layer of the dressing. Cultures from the lower layers of the same yielded abundant growths. At the same time, open

and closed serum tubes were exposed, and eighteen hours after withdrawal were planted with diphtheria and staphylococcus albus. The closed tubes yielded fair growths; the others none.

Next, a series of experiments was begun to determine the value of the agent as a disinfectant for surgical instruments and sutures.

Experiment 1. A director, a probe, several needles, two knives, and a pair of scissors were thoroughly smeared with a bouillon culture of streptococcus, and placed in the cabinet with specimens of catgut of different sizes, two skeins of silk, and two specimens of silk-worm gut. Control cultures made from all the suture specimens yielded abundant growths. Five cc. formalin vaporized into the cabinet completely sterilized everything except the closed scissors after four hours' exposure.

Experiment 2. Test objects: twenty-three specimens of catgut of various sizes, and three specimens of catgut soaked for five days in a bouillon culture of anthrax spores.

Control cultures from each specimen showed abundant growths. The specimens were placed in the cabinet and subjected for two and a half hours to the influence of the vapor from five cc. formalin. Cultures made at the end of that time showed no growths after forty hours, except in two instances. After four days, growths were observed from ten others, the balance remaining sterile. These proved to be mould in six cases, yeast in two, and a spore-bearing bacillus in the remaining two.

After three more days, no further growths were observed among those which were sterile at the last preceding examination. Twenty-four days later one yielded a mould, and another a spore-bearing bacillus.

Experiment 3. Test objects, six specimens of catgut which had been soaked in alcohol and ether, and thoroughly freed from fat, and enclosed in narrow glass tubes with open ends.

Control cultures showed abundant growths from three of the extracted specimens; the others were sterile.

The specimens were placed in the cabinet, and were not removed for three days. Each day, formalin (5 cc.) was introduced in the form of vapor, so that the objects were ex-

posed to three successive disinfections, without any intervals of freedom from the influence of the agent. In other words, they were for three days in an atmosphere of formaldehyde which received additional strength at the end of twenty-four and forty-eight hours from the start.

At the end of three days all were absolutely sterile.

Experiment 4. Six skeins of catgut, C & S, sizes 00, 0, 1, 2, 4 and 5, were cut into pieces about an inch long, and soaked for five days in bouillon culture of sporulating anthrax at 37.5° C. They were then placed in open glass dishes and introduced into a horizontal cylinder of 1,500 cc. capacity, with a hole at one end for the introduction of gas, and a greased ground-glass cover at the other. A glass funnel with the stem bent at a right angle was connected with the orifice mentioned, in such a way as to receive and transmit the formaldehyde liberated by paraformaldehyde pastilles heated in a small Schering lamp.

November 15. Test objects in cylinder subjected to vapor from two pastilles. The glass cover was moved so as to allow a very small outlet during the burning of the lamp.

November 16. Funnel removed and replaced by a test-tube with a side outlet; 1½ cc. formalin vaporized into cylinder.

November 17. One and one-half cc. formalin.

November 19. One and one-half cc. formalin.

A. November 16. (After twenty-four hours' exposure.) Two pieces of each size withdrawn and planted.

B. November 18. (After sixty-five hours' exposure.) Two more of each size withdrawn and planted.

C. November 20. (After four exposures: 120 hours.) Two more of each size withdrawn and planted.

A. Numbers 2 and 5 show growth at end of eleven days (November 27). These proved to be moulds.

B. Number 00 shows mould in nine days (November 27).

C. Everything sterile in seven days (November 27).

Experiment 5. The catgut still remaining in soak in the flasks of anthrax culture was dried in glass dishes at 37.5° C. When dry, controls taken showed abundant growths. The same apparatus as used in Experiment 4 was employed, and the dried pieces were exposed to three successive disinfec-

tions from 1 cc. of formalin, twenty-four hours apart. At the end of each period of twenty-four hours, two pieces of each size were withdrawn and planted, that is, after twenty-four, forty-eight and seventy-two hours (November 23, 24 and 25). The only growths observed from these plantings were three moulds.

Experiment 6. As most of the growths obtained in the preceding experiments had proved to be of moulds, the question arose whether these growths were accidental, as from the cotton stoppers, or whether the moulds were on the sutures and not killed by the gas. Twenty-one moulds were exposed in small glass dishes in the cylinder to the action of 1 cc. formalin on three successive days. All were killed at the first exposure.

The foregoing experiments show that the agent used is a most powerful surface disinfectant, which in a very short time will destroy all known micro-organisms to which it can gain free access; that for room disinfection it is unsurpassed; that it has but little penetrating power, particularly when moisture is present; and that, therefore, it must not be relied upon to sterilize protected organisms and wet objects.

The experiments with catgut demonstrate that that substance can be readily sterilized, but unfortunately for the value of the agent in this direction, it was found on testing the strength and flexibility of the sterilized skeins that these qualities in the smaller sizes were very seriously impaired. Another series of experiments with instruments and sutures has been begun, in which the agent is employed under new and quite different conditions. Thus far the results are most satisfactory in every way, but owing to the length of time which will be required for the completion of the work it will be impossible to put them on record in this communication. They will, therefore, be reported in a later paper.

XIII.

ENDOCARDITIS FROM GONORRHŒA.

By George G. Sears, M.D.

The possibility of malignant endocarditis as a complication of gonorrhœa was clearly shown by a case reported by Brandes as early as 1844. Since then cases with endocardial complications, both simple and malignant, have been reported in considerable numbers, yet, if one may judge from the text-book accounts, they are still looked upon as rare events, while the possibility of the occurrence of the simple form is often left to conjecture.

Osler, who is more than usually explicit, says in the chapter on gonorrhœa "that endocarditis is usually simple, but occasionally there is intense infection and ulcerative endocarditis;" but in the chapter on acute endocarditis, gonorrhœa is not given among the many causes mentioned.

Garrod, in speaking of gonorrhœal rheumatism, which usually, though not invariably, occurs as an antecedent complication in cases which eventuate in endocarditis, says that "one of the most striking differences between gonorrhœal and true rheumatism is the practical immunity of the endocardium in the former disease. It is true that cases are on record in the course of which both pericarditis and endocarditis have occurred, but the very rarity of such records seems to emphasize the rule." He has met with a single case in which a murmur with all the characteristics of mitral regurgitation developed, but it disappeared entirely during convalescence, and might have been hemic. Fagge is even more skeptical, as he says that "gonorrhœal rheumatism and other disorders, which are still vaguely styled rheumatic, show that they have no claim to the title by not producing endocarditis."

A search through the literature of the subject, which it must be confessed was not very thorough, discovered forty-two cases of endocarditis which followed gonorrhœa, and in

which there was little reason to doubt but what the latter had prepared the way by which the infecting agents had entered. They have been grouped together without reference to the special etiological factor, since, however interesting it may be from a pathological standpoint, it is a matter of indifference from the clinical whether the cardiac affection was caused by the gonococcus, or by other pathogenic bacteria, or by a toxine elaborated by them, except in so far as it might influence the prognosis to know the cause, provided that it were possible to determine it during the life of the patient. A few cases have been excluded from the list either because the origin of the murmur seemed doubtful or because the details published were too meagre to be of use.

Another case has recently come under observation of the writer, a brief account of which is given, in order that it may be included in the total number which have been used for analysis, since it does not appear either among the reported cases nor those taken from the hospital records.

The patient, a man twenty-three years of age, was seen in consultation with Dr. G. L. West, of Newton, March 3, 1897. The following day he was removed to the Massachusetts General Hospital, and entered the service of Dr. W. L. Richardson. I am indebted to him for the privilege of using the hospital records of his later history, and to Dr. J. H. Wright for notes of the autopsy.

His family history was negative. His previous health had always been good, except for numerous attacks of gonorrhœa, the last of which came on nine months ago, the discharge still continuing. Three and a half weeks ago he began to complain of pain in the back, stomach and head. He vomited, and had chilly sensations, but no distinct chill. These symptoms have continued with occasional attacks of diarrhœa, and for the past week he has complained of shortness of breath and palpitation. The joints were not affected.

A very loud pre-systolic murmur had developed under the observation of Dr. West, which had suddenly changed during the night preceding my visit, into a harsh systolic murmur, which could be heard over the whole of the lower two-thirds of the left chest. The second pulmonic sound was accentuated. The area of cardiac dulness was not enlarged. A few

coarse moist râles were heard over both chests. The spleen was enlarged. The white blood corpuscles were increased to 20,400.

He became noisy and delirious. There was incontinence of urine and fæces and areas of hemorrhage appeared beneath the skin. The pulse became weaker and more irregular, and the patient grew cyanotic. He finally lapsed into a state of semi-unconsciousness, and died on the ninth. The temperature after he came under observation varied between 99.8° and 105.

The autopsy showed an ulcerative mitral endocarditis with rupture of the valves. Embolic infarctions with abscess formation were present in the left ventricle, in the spleen and kidneys. A stricture of the urethra was found, with dilation and ulceration of the membranous portion, hypertrophy of the bladder and suppurative prostatitis. On bacteriological examination a coccus was found, quite generally distributed, which was unlike in its morphology the ordinary pus producing cocci.

These cases simply prove the fact that endocarditis may result from gonorrhœa, but shed no light on its relative frequency, which can only be obtained by an analysis of a large number of cases, either of gonorrhœa or gonorrhœal rheumatism.

In the hope of gaining more positive evidence on this point, search has been made through the hospital records, but as uncomplicated gonorrhœa is not admitted, this has necessarily been restricted to the cases of gonorrhœal rheumatism, and of these, with one exception, which came under the observation of the writer in consultation with Dr. Lund, the surgeon in charge, only such as were admitted to the medical side have been considered. Effort has been made to exclude all doubtful cases, and therefore all patients whose debilitated, anæmic condition suggested the probability that the murmur was of inorganic origin, and those with a history of previous scarlet fever, rheumatism, or other diseases recognized as productive of endocardial mischief have been thrown out, as well as those with a marked rheumatic family history, unless it was evident that the heart was intact at the time of onset of the original trouble. The possibility that the

joint affection was due to a coincident attack of acute rheumatism, has also been recognized, and a special effort made to eliminate this source of error in view of the fact that in so many cases the arthritis was of the polyarticular form. All cases which obtained marked relief from the use of the salicylates have, therefore, also been excluded.

Since most patients were admitted after the rheumatic symptoms had already existed for several days or weeks, the cardiac damage as represented by the murmur was usually present at the time of admission, and in only a very few did the complication arise under observation. Although this detracts somewhat from the positiveness of the evidence, since the diagnosis must rest on a process of exclusion, yet since no other cause could be discovered, the large proportion found is very striking and suggestive, and would scarcely be expected in a similar number of cases of any disease which has no tendency to attack the endocardium. It is also probable that a murmur may have developed in other cases, but have been overlooked owing to the insidious way in which endocardial lesions come on, or because a lack of interest in such chronic cases, or a want of appreciation that such a complication occurs with sufficient frequency to be watched for, may have led to neglect to constantly examine the heart. These figures, therefore, even if they are not accurate, may approximate the relative frequency.

Out of 167 cases of gonorrhœal rheumatism admitted to the medical wards of the City Hospital between January 1, 1880, and July 1, 1897, twenty-five[1] were found in whom a cardiac murmur was present, for which no other cause than gonorrhœa could be discovered.

In connection with the other cases this gives a total of sixty-eight which may be used for analysis, of whom sixty-one (24)[2] were males and seven (1) females. As was to be expected from the nature of the original trouble, it occurred most frequently in early adult life. The youngest patients, both girls, were respectively ten and twelve years old.

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[1] The proportion does not greatly differ from that given by Nolen, who found endocarditis sixteen times in 115 cases of gonorrhœal arthritis. The original paper was not found.

[2] The number of hospital cases is given throughout in parentheses.

It occurred in a first attack of gonorrhœa in at least thirty-one (13) cases, while in nine others, in which the number was not definitely stated, the attack was also probably the first. It occurred in the second attack in thirteen (8), in the third in three (1), and in the fourth or more in six (3). In six others the number of attacks was not stated.

Although it has become customary to speak of gonorrhœal arthritis, from a supposed analogy to acute rheumatism, as a cause of endocarditis, it is evident that it can only be considered a proof that the infection has extended beyond the primary focus, yet it may perhaps serve to a certain extent as a criterion of the amount of infection or of the susceptibility of the patient. It may not, therefore, be surprising that endocardial inflammation should be more common where many joints are involved, as was shown by the presence of a polyarticular affection in forty-eight (21) of these cases. Nevertheless, it is by no means a necessary complication, as in ten patients it was conspicuously absent. Of the remaining ten cases the arthritis was confined to one joint in four (1), and to two joints also in four (2), while in two cases the number of joints affected was not mentioned.

In thirty-eight (18) cases the mitral valve alone was involved, in twelve (1) the aortic, and in two the pulmonic. The mitral and aortic were both involved in eight (4); the mitral and tricuspid in one; the aortic and pulmonic in one. In one, in addition to a well marked systolic mitral murmur, a double murmur was also heard in the pulmonic area, but the records are not sufficiently explicit for a positive diagnosis. It may have been due to pericardial friction. In five cases the seat of the lesion was not mentioned.

The analysis of the clinical history of those cases shows that endocarditis may come on as early as the second day after the acquirement of gonorrhœa, or as late as the end of a year, provided the discharge still continues, but it much more commonly develops between the third and fifth weeks.

It is at times ushered in by precordial pain or anxiety, as occurred in about one-sixth of these cases, or by a chill with a pronounced rise of temperature, headache, vomiting and pain in the bones, and later either run a course similar to that of malignant endocarditis occurring in other conditions, or

the alarming symptoms may gradually subside, and the disease terminate in recovery, occasionally even with a disappearance of the murmur, or in others the onset may be insidious, without any manifestations referable to the heart, such as occurs in most cases of acute rheumatism, and run an afebrile course.

No very definite line of distinction, however, can be drawn between the clinical histories of the simple and malignant forms, since the former may also be ushered in by a chill, or even by a convulsion, as occurred in one case, and run a stormy course for several days with a high and irregular temperature, while the latter in a few instances produced but a slight disturbance at its onset, and advanced to a fatal issue with only a trifling elevation of temperature. In other words, the simple and malignant cases shaded into each other in their severity, as was to be expected, since we are dealing with the same infecting agents, whose activity must depend upon the quantity of infection and the resisting power of the patients. Nevertheless, the severity of the symptoms, in most instances, gave important indications in prognosis, since in a majority of the fatal cases the cardiac complication was ushered in by grave constitutional disturbance and was very frequently attended by chills, either at the beginning or later in its course, and by a high and irregular temperature, while the simple form rarely showed such serious symptoms. The seat of the lesion would also seem to give valuable information as to the probable outcome, since those cases where the mitral valve alone was attacked showed a decided tendency toward recovery, while the involvement of the aortic or pulmonic valves was generally followed by death. Thus of the forty-three (23) cases which recovered, the lesion was confined to the mitral valve alone in thirty-three (18), and to the aortic in four (1), while in four (3) the aortic and mitral, and in one the mitral and possibly the pulmonic were involved. In one the seat of the lesion was not mentioned. On the other hand, the mitral valve alone was affected in only five of the twenty-five (2) fatal cases, while the aortic was involved in nine (1); the pulmonic in two, the mitral and aortic in four (1); the aortic and pulmonic in one, and the mitral and tricuspid in one. In four the valves affected were not described.

The fatal cases usually ran their course in a few weeks, but it occasionally was protracted over several months, while a few fulminating cases occurred where death resulted in a few days. The longest fatal case ran five months, the shortest nine days after the initial symptoms.

In most of the simple cases the murmur persisted as long as the patient remained under observation, but in a few a well marked murmur, possessing all the characteristics of one due to an organic lesion and accompanied by distinct cardiac symptoms, came on, lasted a few days, and then gradually disappeared, complete recovery apparently ensuing.

An attempt to assign a definite cause for the determination of the infection to the endocardium was made in but a few instances, in some of which cardiac symptoms appeared almost immediately after exposure to cold, while in three they followed so soon after the use of strong urethral injections as to make the connection seem probable.

Apart from the ordinary complications usually found in cases of malignant endocarditis, iritis, pleurisy, pericarditis and purulent myocarditis were occasionally found.

Much interest has centred upon the bacteriology of the secondary infection, but later cases have led to no modification of the conclusions reached by Finger[1] in 1894, which recognized four possibilities, either that the valvular disease is the result of the gonococcus alone, or that the original disease furnishes the way by which pyogenic micrococci also enter and produce a mixed infection, or that the gonococcus primarily invades the endocardium but that pyogenic micrococci enter later and the two exist together, until the former is replaced by the latter, a secondary infection occurring, or that the complication is not due to the actual presence of microbes, but is produced by the products of the development of the gonococcus in the urethra, the offending cause being of a toxic nature.

The latter possibility, which has been very largely theoretical has recently received considerable practical support from some investigations by Wasserman,[2] who has found that the

[1] Arch. F. Derm. u. Syph. 1894, xxviii.
[2] Berl. Klin. Woch., 1897, No. 32.

gonococcus has the power to produce a specific poison, which persists after the death of the micro-organisms, the smallest portions of which, he has proved by experiment, produce inflammation at the point of injection, with fever, swelling of the neighboring glands and severe muscular and joint pains, and against which he has been unable to give immunity to any animal.

An examination of these cases shows that in nine a diplococcus corresponding in all respects in its reactions to that of Neisser, except that it could rarely be cultivated, was found either alone or in combination at the autopsy, and in two cases, which recovered, it was found in the pleural exudate. The ordinary pyogenic cocci were found in a number of other cases, while in others, other forms of cocci which were not completely identified were evidently the cause of the infection.

Points which a study of these cases has served to emphasize may be summarized as follows:

1. Endocarditis is a less infrequent complication of gonorrhœa than is generally supposed. It is possible that a number of cases of valvular murmurs, evidently of long standing, but for which no other etiological factor can be found in their histories, is due to this cause.

2. It appears to be more common in the first than in a later attack of gonorrhœa, but rarely comes on until the discharge has persisted for some weeks.

3. It is usually associated with arthritis, which cannot, however, be considered as an intermediate step, but rather as an evidence of a general infection of which the endocarditis is a part, since it may occur without any involvement of the joints. Nevertheless, it is more common in the polyarticular form of the disease.

4. As a rule the more serious the symptoms the more serious the case, but exceptions may occur.

5. Cases in which the mitral valve alone is affected are much more liable to recover than those in which the aortic alone is affected or where the process has involved two valves.

6. In the fatal cases, death may result in a few days or after several months, the usual course being a few weeks.

7. In the simple cases the murmur usually persists, but occasionally complete recovery ensues.

8. Bacteriologically cases may be due either to infection by the gonococcus alone or to a mixed or secondary infection with other pyogenic organisms. Probably some cases are due to the action of a toxine.

XIV.

HÆMATOPORPHYRINURIA, WITH THE REPORT OF A CASE.

By J. Bergen Ogden, M.D.,

Assistant in Chemistry, Harvard Medical School; Assistant in Clinical Pathology, Boston City Hospital.

Hæmatoporphyrin is a coloring matter which is derived from the blood, and only rarely forms an important constituent of the urine.

The earliest observations bearing upon this subject were made in 1871, when Hoppe-Seyler[1] found that if hæmatin was treated with concentrated sulphuric acid, and heat applied, there resulted a compound whose acid and alkaline solutions showed spectral bands unlike any substance he had seen before. Further experiments convinced him that he was dealing with a new compound, to which he gave the name "hæmatoporphyrin." He forthwith made an effort to determine its chemical composition, arriving at results which were, several years later (1884) found to be incorrect by Nencki and Sieber,[2] who ascertained that its exact chemical formula was $C_{16}\ H_{18}\ N_2\ O_3$.

Nencki[3] found that the only chemical difference between hæmatin and hæmatoporphyrin was, that the latter was hæmatin free from iron.

In 1874 Baumstark[4] described two pigments which he obtained from the urine of a case of leprosy, and to which he gave the names "urorubrohæmatin" and "urofuscohæmatin." The acid solutions of the former gave a spectrum having a very close resemblance to acid hæmatoporphyrin, but the alkaline solutions of this substance failed to yield spectral bands like those of alkaline hæmatoporphyrin. At that time he called attention to the close resemblance of urorubrohæmatin to iron-free hæmatin, but did not regard the two substances identical.

In 1880 MacMunn[5] described a pigment which he obtained from the urine of a case of acute rheumatism, to which he gave the name "urohæmatin." This pigment was found to yield spectral bands which closely resembled hæmatoporphyrin. Three years later[6] (1883) he reported other cases of acute rheumatism whose urine presented this peculiar coloring matter. In a paper[7] published in 1885 he changed the name of this pigment to "urohæmatoporphyrin."

Neusser[8] (1881) described a pigment which he found in the urines of two patients, one of whom was suffering from phthisis pulmonais, and the other from pleurisy with effusion. This pigment was spectroscopically identical with hæmatoporphyrin.

Le Nobel[9] (1887) confirmed MacMunn's observations of the occurrence of a pigment in rheumatic fever, and added that he had met with it in pneumonia and cirrhosis of the liver.

In 1889 Stokvis[10] described a coloring matter which he had found in the urine of a woman who had taken sulphonal.

Ranking and Partington[11] (1890) reported two cases, both females, who showed obscure nervous symptoms. No sulphonal had been taken. The urine of both cases had a deep red color, and contained hæmatoporphyrin.

In the same year von Horley[12] described two cases of hæmatoporphyrinuria, and in both instances sulphonal had been ingested.

Salkowski[13] (1891) reported in detail the chemical and spectral examinations of dark red urines of three patients, all of whom had taken sulphonal.

In 1892 Hammarsten,[14] Goldstein,[15] Sobernheim[16] and Quincke[17] reported cases of hæmatoporphyrinuria following the use of sulphonal. Some of these had taken the drug in large doses for some period, while others had taken only a comparatively small quantity.

Herting[18] (1894) described the urine of a case which had taken both trional and tetronal. It had a dark red color and contained hæmatoporphyrin.

In the same year Schultze[19] reported a case of severe melancholia, in which evening doses of ½ to 1½ grammes of trional had been taken for four weeks — a total of 25 grammes. The urine passed during the fourth week had a muddy, reddish brown appearance, in which the chemical and spectroscopical

examination showed hæmatoporphyrin. A few days later the patient died. There was some question as to whether the trional was the direct cause of death.

Müller,[20] Hearder[21] and others have observed this unusual coloring matter following the ingestion of sulphonal, and all records show that more than a single dose (1 gramme) of the drug had been taken before the coloring matter appeared.

Nakarai[22] (1897) reported the results of 250 examinations of the urine of 144 patients. Hæmatoporphyrin was found in only ten cases, viz.: in all of the six cases of lead poisoning examined, two out of four cases of intestinal tuberculosis, one out of seventeen cases of rheumatism, and once in a case of empyæma following the use of sulphonal. The method employed for the separation of this coloring matter from the urine was that of Salkowski. (See below.)

According to Stokvis,[23] hæmatoporphyrin has also been observed following an intestinal hemorrhage. He succeeded in producing an artificial hæmatoporphyrinuria in rabbits and dogs by giving them sulphonal (0.4 to 0.6 gramme per kilo). He found that the sulphonal, apparently by its irritative action, produced a marked hyperæmia and frequently small hemorrhages into the mucous membrane of the stomach and intestines. From the hemorrhagic areas he was able to extract a coloring matter which, by the spectroscope, was shown to be hæmatoporphyrin. He also found this pigment in the urine of rabbits which had been fed upon fresh meat. His conclusion was that the blood which had entered the digestive tract was first changed to hæmatoporphyrin, then absorbed and eliminated in the urine as such.

Stokvis[24] claims that very small amounts of hæmatoporphyrin can be found in the highly concentrated urine of any healthy person.

Garrod[25] found traces of this pigment in the urines of twenty healthy persons. It was constantly present for a considerable period, but in varying quantities. His observations were confirmed by those of Hopkins.[26]

Salkowski's method[27] *for the separation of hæmatoporphyrin from the urine.*

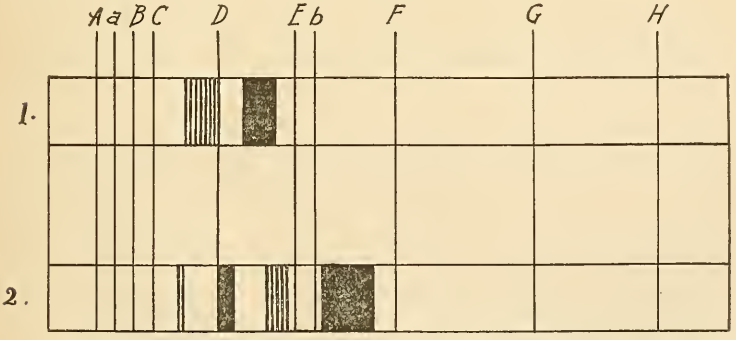
"Take about 30 cc. of urine, add baryta mixture (equal parts of a ten per cent. solution of barium chloride and a saturated solution of barium hydrate), until it is completely

precipitated. Wash once with water, and once with absolute alcohol, using the latter drop by drop. Transfer the precipitate to an evaporating dish, add six to eight drops of concentrated hydrochloric acid and sufficient absolute alcohol to make a thin pap, then stir thoroughly. Heat over a water bath, then filter through a dry filter paper, and add sufficient absolute alcohol to make from eight to ten cc. of filtrate."

This solution (acid) may be examined directly with the spectroscope for the bands of acid hæmatoporphyrin, or may be rendered alkaline, preferably with ammonic hydrate, and examined for the characteristic bands of alkaline hæmatoporphyrin.

It is worthy of note that this alcoholic solution containing the pigment readily decomposes, so that the spectral examinations must be made within a period of two to three days.

Spectrum. The *acid* alcoholic solution shows two absorption bands: one rather dark, situated between Frauenhofer's lines C and D, with its right border on D; and the second, sharply defined, nearly intermediate between D and E. The *alkaline* solution presents a four-banded spectrum as follows: A faint and very narrow band about midway between C and D; two between D and E, one with its left border covering D, the other nearer E; and the fourth band, which is the darkest of all, but which, however, is not well defined, includes about four-fifths of the space between *b* and F, nearer to *b*.



1. Acid Hæmatoporphyrin. 2. Alkaline Hæmatoporphyrin.

H. G., female, thirty-eight, single, having contracted diphtheria, was admitted to the South Department of the Boston City Hospital on November 25, 1896, under the care of Dr. J. H. McCollom.

Her mother and one sister had died of heart disease. She had acute rheumatism at the age of twenty-one (seventeen years ago), at which time a mitral disease of the heart developed.

In the next thirteen years there were four recurrent attacks of rheumatism, which, with the heart disease, required almost constant treatment. She was quite well in the two years previous to the present attack of diphtheria, excepting for palpitation and dyspnœa on exertion.

She had a nervous temperament, and was at times hysterical, having had six or eight hysterical convulsions (eight years ago), following a cessation of the menses. The physical examination showed the heart to be much enlarged, and the presence of a thrill over the precordia. There was a systolic murmur at the apex, transmitted a short distance toward the axilla. There was also a presystolic murmur which was faint but distinct.

Lungs and liver were negative. The abdomen was tympanitic, lax, and quite tender. The extremities were edematous.

There was a diphtheritic membrane on both tonsils. A culture from the throat showed the presence of the Klebs-Loeffler Bacillus. The patient was given antitoxine, and gradually improved, although convalescence was very slow, probably because of the extensive heart disease.

About two weeks later (December 10) she began to have diarrhœa and vomiting, which persisted. Soon after this she complained of pain and tenderness in the legs, which, on examination, was found to be confined to the areas along the nerve trunks.

Urine (December 22): high; strongly acid; sp. gr. 1022; albumin, the *slightest possible trace;* bile and sugar absent. Sediment: a few finely granular and hyaline casts, some with renal epithelium adherent. Considerable squamous and scaly epithelium, few leucocytes, and an occasional normal blood globule. The urine chart showed the twenty-four hour quantity to vary between 450 and 600 cc.

On December 15 the patient was discharged from the South Department and admitted to the wards of the main hospital on the service of Dr. G. B. Shattuck, and later that of Dr. C. F. Withington.

About this time she began to lose sensation in the legs; this was followed (two weeks later) with almost complete loss of sensation up to the waist line, accompanied by involuntary micturition and dejections. The pain on pressure over the nerve trunks was extreme. Patellar reflexes diminished, but present. General muscular atrophy. Diarrhœa persistent; frequent attacks of vomiting. Free, and at times, profuse perspiration.

On or about February 10 the urine was found to be very scanty in amount, but on account of the involuntary micturition it could not be collected. On February 12, however, a small catheter specimen was obtained which had the following characteristics: Color, very dark, resembling port wine; sp. gr., 1025; reaction, strongly acid; urophæin and indoxyl much increased; chlorides and phosphates much diminished; urea, 3.15 per cent.; albumin, a very slight trace (heat test); bile and sugar absent. The sediment was abundant in quantity, and consisted of a deposit of amorphous urates and a few uric acid crystals. Some squamous epithelium and a few pus corpuscles. An occasional brown granular cast, and rarely a blood globule. A little fat found adherent to an occasional cast.

No more urine could be obtained, in fact very little was secreted. The patient gradually lost strength, and died on the morning of February 14. An autopsy could not be obtained.

The treatment consisted chiefly of heart tonics, such as tincture digitalis, tincture strophanthus, strychnine, etc. Bismuth and salol were from time to time given for the diarrhœa, but none within four weeks of the time of death. At two different times (January 31 and February 6) 15-grain doses of trional were given for insomnia.

The dark red urine which was collected on February 12 was examined with the spectroscope. At first, the untreated urine (acid) was used, but with unsatisfactory results, since the two spectral bands of acid hæmatoporphyrin could not be made out with certainty. The pigment was then separated from the urine by Salkowski's method (see above), and it was found that both the acid and alkaline solutions gave the characteristic absorption bands of hæmatoporphyrin.

The trional which had been taken was probably the cause of the unusual pigment in the urine of this case, although there is some doubt; first of all, on account of the length of time which elapsed (eleven and five days respectively) between the ingestion of the drug and the discovery of the hæmatoporphyrin in the urine; and secondly, the inability to collect and carefully examine the urine after the trional had been taken.

Whether the disease of the nervous system, and the marked gastro-intestinal disturbance in the case had any bearing upon the cause of the hæmatoporphyrinuria is not known, although such a possibility exists.

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XV.

A STUDY OF THIRTY-SEVEN FATAL CASES OF CIRRHOSIS OF THE LIVER.

By John Lovett Morse, M.D.

Considerable confusion exists not only pathologically and ætiologically but also clinically as to the classification of cirrhosis of the liver. The cases may, in a general way, be divided into two main classes, according as the size of the liver is diminished or increased. The first is usually spoken of as atrophic; the second as cirrhosis with enlargement or hypertrophic. Both are the result of an abnormal development of connective tissue; in one case contraction being a prominent feature, in the other not. In both also, various changes of greater or less extent, probably secondary in origin, occur in the liver cells. The former conception of atrophic cirrhosis with its attendant symptoms as the result of the overgrowth of the connective tissue of the portal system only, and of hypertrophic as the result of that of the biliary system only, cannot now be accepted but in a greatly modified form, as the process is always a more complex one. The division into interlobular and intralobular forms is also indefinite as both conditions invariably occur together.

The great majority of the contracted livers are probably due to alcohol, although a certain number are the result of the same agents which produce the large livers or of other influences at present unknown. Hanot's classification of cirrhosis with enlargement from the standpoint of ætiology is perhaps as satisfactory as any: malarial, syphilitic, tuberculous, biliary from retention, alcoholic, fatty alcoholic, and finally, perhaps belonging in a separate class, the hypertrophic cirrhosis with chronic icterus.

While there is a pretty general agreement among medical writers as to the symptomatology of the ordinary forms of

cirrhosis with contraction and cirrhosis with enlargement there seems to be considerable confusion regarding that of the form described by Hanot as hypertrophic cirrhosis with chronic icterus. In fact, many writers doubt even the existence of such a form. Hence, it may be well to give briefly Hanot's own description. It usually occurs in young and feeble men, beginning with an attack of pain in the right hypochondrium, associated with symptoms of disturbed digestion. This is soon followed by jaundice, which is persistent and gradually increases. Crises of pain and indigestion occur at intervals, but at other times there are no symptoms. Enlargement of both liver and spleen begins early, and is progressive, both becoming enormous. There is no ascites or venous enlargement, and the fæces remain of normal color. The nutrition is maintained unimpaired for a long time, cachexia rarely appearing under four years. The course is from two to twelve years, more often the longer period. The cause is obscure, although alcohol, syphilis, malaria and lithiasis have seemed of ætiological importance in some cases.

It was with the hope that something of interest might be learned concerning the ætiology and symptomatology of these somewhat obscure conditions that this study was undertaken, and the medical records of the Boston City Hospital for the seventeen years ending with 1896 investigated. During this period 50,347 cases, exclusive of diphtheria and scarlet fever, were admitted to the medical wards. In 333 of these, or 0.66 per cent., the diagnosis of cirrhosis of the liver, either as the principal or as a complicating condition, was made. In the nearly 2,000 autopsies made on medical cases, exclusive of diphtheria and scarlet fever, during this same period, the clinical diagnosis of cirrhosis of the liver was confirmed in thirty-seven. On account of the difficulty in the diagnosis of this condition, and of the uncertainty inherent in all diagnoses unconfirmed by post-mortem examination, it seemed best to study only the autopsied cases.

For convenience of comparison they have been divided into three classes, according to the size of the liver as determined at autopsy. The first comprises the livers larger than normal, the second those of a size within normal limits,

and the third those smaller than normal. It is possible that those of normal size should be considered with the small ones rather than in a class by themselves. It may be of interest to note that clinically the increased size of the liver was always recognized, and that its irregularity was occasionally noted. The livers of normal size, however, were usually considered large, while the diminution in size was recognized in about half the cases. The pathological data are, unfortunately, nearly all microscopic and of little use except in establishing the diagnosis of an increase of connective tissue with greater or less destruction of liver tissue and increase of fat. Chronic perihepatitis was noted in one of the large livers, in four of those of normal size, and in three of the small. The following table shows some interesting general points: It appears from this table that cirrhosis with enlargement, without change in size and with diminution in size, are equally frequent, and that the size of the liver is increased in a third of the cases. The male sex is more frequently affected. Cirrhosis with enlargement is more common in younger people, and cirrhosis with atrophy in old. The average duration of symptoms is longer in the atrophic cases. The duration of symptoms, however, varies within wide limits in all varieties. Hæmorrhage is a not infrequent cause of death in all forms, and a fatal hæmorrhage may be the first symptom even in the hypertrophic form. An alcoholic history was obtained in every case in which the subject was investigated. A history of previous malaria, syphilis or gall stones was occasionally obtained, but in none did it seem of ætiologic importance.

	Large Livers.	Normal-Sized Livers.	Small Livers.
Number of cases	13	11	13
Average age at death	40	52	49
Sex	Males 9 Females 4	Males 6 Females 5	Males 8 Females 5
Average duration from first symptom in cases in which death not due to complication [1]	In eight cases 14 mos. Shortest 8 " Longest 30 "	In six cases 9 mos. Shortest 3 " Longest 24 "	In ten cases 25 mos. Shortest 3 " Longest 72 "
Cause of death	Stress of disease 10 Hæmorrhage 1 Complications 2	Stress of disease 8 Hæmorrhage 2 Œdema of brain 1	Stress of disease 9 Hæmorrhage 2 Complications 2
Cause of disease	Alcoholic history 13 No Data as to alcohol 0 History of syphilis in 1 and gall stones in 2. Gall stones not of importance as ducts free.	Alcoholic history 6 No Data as to alcohol 5 History of syphilis 1 " " Malaria 1 (Non-alcoholic cases.)	Alcoholic history 11 No data as to alcohol 2 History of malaria 2 (Both alcoholic cases.)

[1] In one each of the large and normal classes a fatal hæmorrhage was the first symptom.

In the following table the individual symptoms and their relative frequency in the different classes are considered. As complete data were often wanting in the records it seemed best to also compare percentages made up only from the cases in which the data were complete.

Symptoms.	Large — 13.		Normal — 11.		Small — 13.		Total — 37.	
	Absolute Number.	Percentage.	Absolute Number.	Percentage.	Absolute Number.	Percentage.	Absolute Number.	Percentage.
Ascites — Present in.....	5	39%	8	73%	10	77%	23	62%
Average duration of...	5 months	.....	6 months	.....	4 months	.....	5 months	
Shortest duration of ...	1 month	.....	5 weeks	.....	3 weeks			
Longest duration of	1 year	.....	2 years	.....	1 year			
First symptom	0	.....	4	36%	1	8%	5	14%
Jaundice[1] — Present in ..	9	69%	5	45%	8[2]	61%	22	59%
Average duration of ...	5 months	.....	2 months	... ..	3 mos.[3]			
First symptom.....	1	8%	0	.....	0	.....	1	3%
Without ascites	4	31%	0	.....	2	15%	6	16%
Preceded ascites	2	15%	0	.....	1	8%	3	8%
Followed ascites.....	3	23%	5	45%	5	39%	13	35%
Large veins — Present in,	3	60%	1	17%	4	31%	8	40%
Abdominal.....	3	.....	1	.....	3			
Hæmorrhoidal	1	....[4].	1	.....	1			
Hæmorrhage[4]	2	15%	3	27%	3	23%	8	22%
Vomitus.....	2	.....	3	. ....	2	.....	7	
Stools	1	.....	3	.....	3	.....	7	
Indigestion	6	75%	7	100%	7	89%	20	87%
Slight	2	.....	3	.....	2			
Moderate.....	2	.....	1	.....	3			
Marked	2	.....	2	.....	1			
Average duration of....	7 months	.....	5 months	.....	6 months			
First symptom	3	37%	1	14%	1	13%	5	25%
Nutrition — Good	12	100%	7	70%	9	75%	28	82%
Poor	0	.....	3	30%	3	25%	6	18%

[1] Clay-colored stools in two of large and one of normal class.
[2] In four of these cases it was noted that the bile-ducts were patent.
[3] In several others at intervals for two to six years.
[4] Source of hæmorrhage was œsophageal veins in two; duodenal in one; ileal in one, and hæmorrhoidal in one.

Among other symptoms pain in the region of the liver was mentioned two or three times in each class, but tenderness was never noted. Swelling of the feet and dyspnœa were very common early symptoms in all forms, often preceding any others by months. Late in the disease anasarca and accumulations of fluid in the various serous cavities often developed. Delirium or coma, and in one case convulsions, often preceded for a few weeks the fatal termination. The brain was examined in several of these cases, and nothing abnormal found except in one case where there was edema. The brain in the case of convulsions was normal. There seemed, however, to be rather a definite relation between the nervous symptoms and jaundice.

An analysis of this table shows the following facts: Ascites was about half as frequent in the cases with hepatic enlargement as in the others, in which it was sometimes the first symptom noted. In all forms, however, it was, as a rule, rather a late symptom. Jaundice occurred, sooner or later, in more than half of all the cases: more often, however, in the cases with hypertrophy in which it also, as a rule, occurred earlier and lasted longer. In the hypertrophic form it often occurred in cases in which ascites never developed, rarely without ascites in the others. It sometimes preceded ascites, especially in the cases with enlargement, but more often followed it. The abdominal veins were dilated in somewhat less than half of all the cases; proportionately more in the hypertrophic form. Hæmorrhages from the alimentary tract occurred in about one-quarter of the cases, but were less common in the cases with enlargement. Indigestion was more or less troublesome in all forms, being one of the earliest and most persistent symptoms. The nutrition was retained practically unimpaired in all the cases with hepatic enlargement and in about three-quarters of the others.

The inconstancy of the symptoms and the irregularity of their development, both absolutely and relatively, is most striking. In comparison with the others the cases with hepatic enlargement maintained their nutrition better, had jaundice more frequently and earlier, developed ascites less often and later, and were less subject to hemorrhage. It is

to be noted that none of the cases resembled in their symptomatology the hypertrophic cirrhosis with chronic icterus of Hanot.

The size and condition of the spleen seems worthy of special attention. It was of normal size in one and enlarged in twelve of the cases with hepatic enlargement; normal in two, and enlarged in nine of the normal-sized livers; normal in three, and enlarged in ten of the atrophic form. The maximum weights were respectively 1,200, 600 and 1,200 grammes. No relation was evident in any form between the size of the spleen and the duration of the symptoms or the amount or duration of the ascites. Three of the cases with hepatic atrophy with marked ascites showed no splenic enlargement. On the other hand some of the largest spleens were found in cases in which there was no ascites. Moreover, the spleen was enlarged in most and of increased density in all of the cases in which death occurred early from complications. Unfortunately, no microscopic examinations of the spleens were made. The condition was often described as passive congestion, and sometimes as a hyperplasia of the pulp. Chronic perisplenitis was present in four of the first, three of the second and six of the third class. The early development of splenic enlargement and the apparent independence of ascites and splenic enlargement of each other seem to suggest some other or additional cause for the enlargement than portal congestion. This discrepancy has already been noted by Oestreich who, after a careful study of the clinical histories, autopsies and microscopical examinations of the livers and spleens of early and late cases of cirrhosis, comes to the conclusion that "the existence of the splenic tumor in cirrhosis of the liver is independent of the liver and due to irritative processes." The irritant is the same as that which causes the diseased process in the liver.

The associated chronic complications in the other organs were as follows:

Complications.	Large—13.	Normal—11.	Small—13.	Total—37.
Heart—Hypertrophy Left Ventricle	3	3	3	9
Fatty Degeneration	2	3	.....	5
Fibrous Myocarditis	1	.....	.....	1
Chronic Fibrous Pericarditis	1	1	1	3
Arteries—Chronic Endaortitis	3	4	4	11
Lungs—Tuberculosis, Active	.....	.....	2	2
Healed	.....	2	1	3
Chronic Bronchitis	.....	2	1	3
Pleura—Acute Fibrinous Pleurisy	.....	.....	1	1
Chronic Adhesive Pleurisy	2	2	4	8
Gastro-Intestinal Canal—				
Chronic Passive Congestion	2	1	.....	3
Chronic Gastric Catarrh	1	1	1	3
Dilation of Oesophageal Veins	1	.....	1	2
Dilatation of Duodenal Veins	1	.....	.....	1
Peritoneum—Chronic Peritonitis	.....	2	1	3
Pancreas—Chronic Interstitial Pancreatitis	.....	.....	1	1
Kidneys—Passive Congestion	3	1	3	7
Chronic Diffuse Nephritis	3	2	1	6
Chronic Interstitial Nephritis	2	4	3	9

These figures agree in a general way with those of Lange, based on a considerably larger number of cases. They show, as do his, a marked tendency to interstitial changes in the serous membranes, kidneys and general arterial system. They are presumably due to the same cause as those in the liver and spleen. The pathological changes in the gastro-enteric tract are surprisingly small for a disease in which portal congestion is supposed to play so large a part.

The preceding statistics justify to a certain extent the following conclusions: Cirrhosis of the liver is a comparatively rare disease. It is the result, in the vast majority of cases, of the abuse of alcohol. Alcohol may cause either an increase or a diminution in the size of the liver. Both are due to the abnormal development of connective tissue. Why hypertrophy results in one case and atrophy in another is at present unknown. All forms have the same symptoms. There is no regularity in the relative development of these symptoms. The sequence, however, varies to a certain extent in the different forms. Portal congestion plays a less important part in the development of these symptoms than is generally supposed. Many of the associated lesions are of the same nature as those in the liver, and are due to the same cause.

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XVI.

A CASE OF MALIGNANT PUSTULE.

By Abner Post, M.D., *Visiting Surgeon.*

On Wednesday, June 23, 1897, about noon, D. W. H. was admitted to the hospital as a case of anthrax. The diagnosis had been made by Dr. Richard E. Edes, who had seen the patient earlier in the morning, and had identified the bacillus before sending him to the hospital.

The characteristic "pustule" was to be seen on the neck. It consisted of an oval gangrenous spot or eschar about the size of a five-cent piece, surrounded by a vesicular border, with edema and induration extending down the neck. It was situated on the right side, midway between the angle of the jaw and the clavicle. The patient was stupid, and evidently only partially conscious, but could be easily aroused. He was incoherent in his answers to questions and while we watched him upon the accident table he had an epileptiform convulsion, beginning with the hands and accompanied by an involuntary dejection.

The man was evidently suffering from severe systemic infection, and seemed already beyond human aid, but in view of the beneficial effects attributed to excision even in apparently desperate cases, the eschar, with its areola, was promptly excised.

The excision was quickly and easily done, but without noticeable effect upon the condition of the patient who had another convulsion later in the day, and died about nine o'clock the same night.

He was a porter in a leather warehouse and accustomed to carry hides upon his shoulders. He had recently been carrying hides of an unusual character, and it was thought they might be the source of the infection.

Saturday morning when shaving he first noticed a small "pimple" in the neck, but considered it of no consequence.

He worked on Saturday and Monday. Went to work Tuesday, but was obliged to return home during the morning with no marked symptom except that he was tired out, and as stated above was admitted to the hospital on Wednesday.

In all probability the little "pimple," seen on Saturday and cut by the razor, was the first manifestation on the skin of the disease rather than the spot which was inoculated subsequent to the razor cut. That would place the patient's death upon the fifth day of the external manifestation.[1] It was impossible to say whether the intestinal ulcers revealed at the autopsy or the cutaneous eschar were the older. Probably there was very little difference in age.

There seem to have been no symptoms that gave any clue to the intestinal lesions, except a degree of constitutional disturbance out of all proportion to the external signs. The involuntary dejection during the first convulsion could hardly be looked upon as suggesting intestinal ulceration.

After the post-mortem examination had revealed the intestinal lesions, Drs. Curry and Mann learned the following interesting facts: That the patient was usually extremely neat in his habits about eating, but of late he had suffered from an inflamed tooth and had frequently carried his fingers into his mouth to ease the pain. Probably this is the explanation of the numerous intestinal inoculations.

The search for the source of the infection was very thorough, but was entirely negative in result. Drs. Mann and Curry visited the place where the man worked and obtained specimens of various hides from the lots which the patient had handled, and also several "swabs" from the floor, but in none of these specimens was the anthrax bacillus found.

D. W. H., Ward K, 9, bed 1, 3d Surg. Autopsy, June 25, 1897, by Dr. Mallory. Clinical Diagnosis — Anthrax. Body of a tall, well-built and well-nourished man, about forty years of age. Operation wound over right mastoid, sealed with collodion dressing. Considerable lividity of neck, upper part of thorax and dependent portions of body.

In the peritoneal cavity a small amount of light reddish fluid. In the mesentery everywhere, in patches in the

[1] The chief interest in the case centres in the intestinal lesions which are described by Dr. Mallory below and which explain the extreme severity and fatal issue.

intestine, beneath the peritoneum of the flanks, and over the bladder were numerous gas bubbles; some of the air cavities were as large as peas.

The intestines were moderately distended, here and there in the ileum were dark hæmorrhagic areas from 1 to 3 cm. in diameter.

Pleural cavities: fibrous adhesions on right side over the upper lobe, on the left side over both upper and lower lobes.

Peritoneal cavity contained about 20 cc. of a light reddish fluid.

Heart: weight, 360 grammes. Flabby; contained dark, viscid, almost tarry blood. Valves and aorta stained red with blood. Valves normal.

Lungs deeply injected, somewhat edematous, especially posteriorly.

Spleen considerably enlarged, weight, 340 grammes. Fairly firm; on section rather dark in color; pulp much increased. Follicles not visible.

Kidneys, combined weight, 385 grammes; showed nothing beyond considerable injection.

Bladder contained a small amount of urine. Testicles normal.

Gastro-intestinal tract. In the stomach, just below the cardiac orifice, was an irregular solid tumor mass beneath the mucous membrane measuring 2 by 3 cm. At the pyloric orifice were two small, round clean ulcers about 1 cm. in diameter which extended into the muscular coat. Edges not indurated. In the small intestine beginning 7 cm. from the pylorus and extending almost to the ileo-cæcal valve was a series of dark hæmorrhagic areas varying from 4 to 15 mm. in diameter. The centre of each area was thicker than the periphery and was covered with a slight grayish, ragged membrane. Outside of the deep dark hæmorrhagic areas were occasional masses of gas bubbles in the tissue. None of these areas were found in the large intestine.

Liver: weight, 1,860 grammes. Much injected. In places were numerous lighter areas beneath the capsule and in the substance of the liver filled with small bubbles of gas.

The blood in the portal vein and inferior vena cava was dark, tarry, and contained bubbles of gas.

Brain: extensive hæmorrhage was present all over the surface of the brain including the base, lying for the most part in the meshes of the pia. It varied from 1 to 3 mm. in thickness and seemed to come from no single source. On opening the ventricles quite a little clotted blood was found in the lateral ventricles. On sectioning the brain multiple punctate hæmorrhages were found; most numerous in the corpus striatum on the right side.

Cover-slip preparations from the brain showed numerous anthrax bacilli. They were also found in the heart's blood on the right side; in the blood in the aorta and in the spleen.

Anatomical Diagnosis. — Anthrax. Primary infection of neck and of intestines. Acute splenic tumor. Congestion of lungs, kidney and liver. Multiple hæmorrhages in meninges and brain substance.

Anatomical specimen, removed June 23, consisted of a central, slightly sunken dull purple portion 5 by 1 cm., over which there is a thin yellow membrane resembling dead skin; no distinct ulceration. About this is an area of very small vesicles with bloody serous contents. The whole mass 2 by 1 cm. is very prominent, shows a marked purplish color, and is surrounded by an area of induration 1 cm. broad which merges into normal skin.

Gross sections were not made; whole mass being hardened in Zenker's fluid.

Smears from vesicles about pustule show fairly abundant large bacilli in chains of a few elements or singly. Bacilli are square ended, and when in chains show a slight cupping of either end, leaving a chink between ends of rods.

Cultures from vesicles and anterior edge of wound showed, in twenty-four hours, abundant growth of irregular, rough, rather flat colonies which, under a low power, showed as wavy, entangled filaments giving edge of colony a feathery outline. Microscopic examination showed large bacilli in long chains. In places the chains are apparently solid; in places divisions can be sharply made out, and in places narrow oval chinks are seen between the individuals in the chains. Many of the organisms show a central oval portion which is sharply outlined, and which does not stain. Cultures made from the depth of the wound show no growth.

Microscopic examination of sections of the skin shows very extensive hæmorrhage and purulent infiltration of the subcutaneous tissue. A large part of it, however, seems to be directly within the skin, the epithelial cells being forced apart by the other cells. There are a few lymphoid cells among the pus cells, but there is no evidence of cell proliferation. In the lower part of the tissue there is extensive edema.

Smears from heart showed abundant short chains of anthrax, and many large bacilli, with rounded ends, occurring in chains and large filaments, and in some cases producing spores.

Smears and frozen sections from spleen showed the same large spore-bearing bacillus, and few short chains of anthrax. Smears from brain (membranes) showed abundant anthrax, and very rarely the large spore bearer with rounded ends.

Cultures. Heart: several colonies anthrax; few streptococci.

Liver: two colonies anthrax; abundant growth of colon.

Spleen: several colonies of anthrax. Stab cultures showed abundant growth of a large spore forming, gas producing bacillus which did not grow on serum tubes.

Kidney: three colonies anthrax, pneumococcus, staphylococcus albus and citreous, colon.

Right lung: pneumococcus, streptococcus and colon bacillus.

Left lung: one colony anthrax, pneumococcus and colon bacillus.

Urine: abundant varied growth, colon, staphylococcus albus and streptococcus present.

MICROSCOPIC EXAMINATION.

Intestine.—Section of one of the hæmorrhagic masses in the small intestine shows with a low power desquamation of the surface epithelium and enormous hæmorrhage, necrosis and purulent inflammation of the mucous membrane. In the subcutaneous tissue the blood vessels contain large numbers of pus cells, and there is cellular infiltration, hæmorrhage and edema extending down to the peritoneum. In some of the small arteries the intima is elevated and beneath the intima there is a large space containing pus cells and large epitheloid

cells. In the vein there is purulent infiltration of the wall of the vein and the endothelium seems to be generally raised and broken through. Emigration of leucocytes through the vein walls is extremely active. In a comparatively thick vein the nucleus of an emigrated leucocyte frequently stretches entirely through the vein wall. The leucocytes appear to be coming through the vein in definite places. The vein principally contains definite polynuclear leucocytes, but among these there are numbers of large leucocytes with an epitheloid looking nucleus. There are great numbers of anthrax bacilli in the submucous tissue. There does not seem to be any very marked change in the mucous membrane in the vicinity of the pustules. In the mucous surface of the pustule the process is somewhat obscured by the hæmorrhage. There is very little evidence of proliferation of the tissue, with the exception of slight swelling of the endothelium of the blood vessels in some places. The cells are entirely pus cells. There is no formation of plasma cells. Another pustule of the small intestine shows essentially the same process, but in this the hæmorrhage is more marked than in the first case, and there is less involvement of the submucous tissue. The anthrax bacilli are, to a large extent, in the edematous submucosa and have grown out into long threads.

Section of the duodenum shows a typical gastric ulcer, with perfectly smooth edges extending down into the muscular coat with no evidence of inflammation about it.

Section of the brain shows in the meninges an intense hæmorrhagic purulent infiltration. The blood vessels are dilated and large numbers of leucocytes are in their walls. The bacilli are more numerous in the meninges than elsewhere. There is a general infiltration of pus cells and among the typical polynuclear leucocytes there are large numbers of cells with a round or slightly curved vesicular nucleus, evidently corresponding to the so-called large transitional forms. Fibrin is present in variable amount. Elsewhere in the brain there are foci of hæmorrhage at various points. Large numbers of anthrax bacilli are found here, and intense purulent infiltration in places. Occasionally, around the vessels, the anthrax bacilli are packed in close masses.

Section of the liver shows considerable fatty infiltration of the liver cells, and there are considerable numbers of anthrax bacilli usually taking the form of long threads in the capillaries.

In the spleen the malpighian bodies are not sharply circumscribed. There is a great deal of hæmorrhage in the tissue, comparatively few leucocytes and some formation of plasma cells.

Sections of the kidney show a marked degree of swelling and degeneration of the epithelium, and œdema of the interstitial tissue, and there are scattered anthrax bacilli everywhere.

Sections of the lung show œdema.

XVII.

A CASE OF LATE CONGENITAL SYPHILIS.

By Abner Post, M.D., Visiting Surgeon.
With Autopsy by W. T. Councilman, M.D., Visiting Pathologist.

This case possesses so many points of interest that the history is given at some length and almost without variation from the hospital record, even including some matters that seem irrevelant. I first saw the patient on December 12. He was not noticeably inferior to others in physique though he must have been slightly below normal in weight and muscular development. His features were not irregular, nor was he specially noticeable, in all probability, to his comrades. In fact, his nose was straight and prominent, and his head not misshapen.

When my attention was once attracted to him he was seen to present a typical picture of late inherited syphilis. He was both quite deaf and nearly blind. The blindness was easily recognized as due to opacities in the corneæ. The teeth needed to be looked at closely to discover any special peculiarity, but close inspection showed a perfect, though not prominent, Hutchinsonian deformity. The grooved edge of the incisors was not particularly deep; it was doubtless worn away somewhat, but these three conditions were present together — partial blindness, deafness and deformity of the upper middle incisors — forming the so-called Hutchinsonian triad. Further investigation showed a throat which had suffered from rather extensive ulceration and loss of substance. In addition, the little scars at the corners of the mouth, which are the result of ulcers in early life, were quite well marked. There was also present a deformity in the jaws, which was of some value in connection with other signs. His middle incisors in the two jaws failed to meet, because of a lack of

development in the upper jaw. This is a deformity to which attention was first drawn by Mr. Coleman, the dentist, who examined, with Mr. Hutchinson, some of the early examples of deformed teeth which Mr. Hutchinson reported. This peculiarity is well shown in the photograph. The Hutchinsonian triad, with the other peculiarities mentioned, presented the signs which are distinctive of hereditary disease. The history confirms the diagnosis made first from the record found on his person. There is, however, one peculiarity in that history, namely, that he is the eldest child, and survived, while the following two pregnancies resulted in abortions.

—— ——, twenty-two, single, entered hospital for the second time, Nov. 25, 1895, in the service of Dr. Folsom, who most kindly gave me permission to study the case.

Parents, five sisters and two brothers, alive, and said to be well. Two sisters have died, one of pneumonia at one year old, the other of "congestion of the stomach." No history of tuberculosis in ancestors of either parent and, at the time the history was taken there was no history of disease in either parent to be obtained. Mother had two miscarriages *following* birth of patient, who was first child. Both miscarriages at about sixth month. Next child born when patient was four years old.

Past history of the patient was given by his mother as follows: When a week old had sores at corners of his mouth and about eyes, and again at four years a similar eruption not associated with measles which he had at the same age. These lesions were covered with crusts. No eruptions on other parts of body so far as known. About seven years old he had some trouble with his eyes, apparently interstitial keratitis; they became red and he was nearly blind; could see light, but could not recognize people.

This lasted two years; sight slowly returned, but remained very "near sighted" afterwards. As the eyes grew better the ears became affected, and in about a year he was practically deaf for all but very loud sounds. He was a fairly strong boy at this age, but has always been somewhat "delicate."

From ten to sixteen years of age he was about as strong as boys usually are. At sixteen he had swelling and pain in legs from knees down.

First entered hospital March 15, 1892, under Dr. Mason, complaining of pain in right umbilical and in cardiac region. Some loss of flesh and constipation. No cough.

Physical examination: Well developed and nourished. Double iritis. Pale. Heart and lungs negative.

Abdomen: Dulness in epigastrium to right of median line extending about two inches below rib margins.

Resistance on deep pressure. Some tenderness on pressure in iliac region, and simply more fulness on right than on left.

Liver: some enlargement.

Spleen: negative.

Glands: some enlarged glands in groins, and in back of neck and above elbow.

March 18, Dr. Wadsworth reports: Double choroiditis and old double keratitis, probably specific origin.

Two years ago a lump appeared on back of neck. Other lumps had appeared in last six months on each side of neck. Said to be more elsewhere. These have never been painful or broken down or softened or suppurated.

Present illness: Almost a year ago he had a good deal of stomach ache lasting about an hour after meals; his appetite was enormous, color fairly good. He did not vomit, but had some nausea. There was no swelling or tumor noticed, The bowels were regular, and he was in his usual health, except for stomach aches.

About April 1, 1895, noticed swelling and a tumor about region of right hypochondrium where it joins epigastric region. This tumor not recognized by him as rough; it projected and was about the size of the fist. Rest of abdomen not much distended. This tumor increased gradually in size and has never diminished as far as known. With appearance of tumor his legs began to swell from knees down. The swelling has gone down at times and reappeared again. Is still present at entrance.

Diarrhœa appeared with other symptoms; five or six movements a day. Soft but not watery, normal in color, no blood seen. No jaundice seen. Diarrhœa has continued to time of entrance. He has been as bright as usual about his work and his color and general condition as regards nutrition

are about as usual. It may be that he has lost a little in weight. His work has been interrupted on account of lack of business, but he has worked until six weeks ago, when he stopped on account of pain, swelling and weakness of legs. Appetite has been large until week before entrance, and good during past week. Patient went to Medical Out-Patient Department Oct. 3, 1895, until which time had had no medicine. After this made about one visit a week to Out-Patient Department. Abdominal measurement was then 34 inches. (December 1, 33½, and December 8, 34 inches.) A week before he came to hospital severe pain in back came on; he had not had this before to any extent. Also pain in limbs became more severe. He was not confined to house before this, but has been on bed or lounge since. Three or four days before entrance he had severe abdominal pain, lasting about two and one-half hours. Has slept well, until a week ago, when pain has kept him awake; he enters with tumor, not diminished in size, not tender or painful, and his chief complaint is of pains in back and legs. Never had cough.

Liver upper limit at fifth interspace. In epigastrium beginning at ensiform cartilage and extending downward four and one-half inches is a hard mass and definite lower edge, and extending to the right and to the left a considerable distance, being nine inches in width. The right half of the mass is nodular and the left smooth. The lower edge descends with respiration. The mass not tender to touch. Veins of abdomen and chest prominent. Whole abdomen much distended and dull in flanks.

Spleen enlarged to percussion. Edge felt two inches below costal margin.

Extremities: both knees swollen and tender.

Glands: much enlarged in back of neck, some enlargement in supra clavicular fossæ. No axillary or inguinal enlargement.

Throat shows general redness and glazed appearance. Numerous small cicatrices about soft palate and pillars of fauces. Posterior pillars of both sides are bound to posterior pharyngeal wall by old cicatricial adhesions, leaving only a small chink leading from pharynx to naso-pharynx. Uvula

free. On left posterior pillar a small pinched out area with smooth edges, size of end of finger.

November 30. There has been no change in tumor since entrance. Veins of both knees distended. Knees slightly swollen. Pain in back and knees, worse at night. Appetite very good. No diarrhœa. Feels better sitting up. No pain or distress after eating. Sleeps well. Still pain in knees. Knees less swollen and pain less severe. No vomiting. Good appetite for one who is inactive.

December 12. Sleep has been fairly good until two nights ago. Attributes insomnia to restlessness rather than pain. Less swelling in legs, can walk fairly well. Slight effusion into both knee joints. Mobility good in right. No tenderness anywhere. Eyes examined by Dr. Lancaster. Old interstitial keratitis which has left grayish, somewhat diffuse, opacity of both corneæ. Old iritis leaving posterior synechiæ in both eyes and some deposits on lens over pupil of left eye. Old disseminated choroiditis of both eyes. Unusually complete picture of hereditary syphilis as it affects the eyes.

December 20. Diarrhœa keeps up. Some effusion remains in joints.

December 21. To-day patient's temperature shot up after being regular for past few days. His head began to ache. A small indurated red area appeared over right ulna, painful and tender, and red lines spread from up and down forearm. Also much the same appearance on left thigh where the red area was more diffuse. Both processes seem to involve the subcutaneous tissue. Slept well last night, but to-night skin is very hot and he is very uncomfortable.

December 24. Urine: color dark brown: Sp. Gr. (not enough urine obtained). Acid. Albumen $\frac{1}{10}$ per cent. Sediment: A great many abnormal blood cells, some in clumps. A few normal blood cells. Hyaline and fine granular casts, some with fat adherent. Epithelial casts. Small round cells in clumps. A moderate number of leucocytes.

December 23. Vomiting became excessive. Unable to retain anything. Good deal of nausea and retching without vomiting even when he had taken no food. Vomitus when mixed with food is green and watery. Pulse still good, fairly strong.

December 24. Stupid, dull, with eyes partly closed; intense jaundice; conjunctivæ yellow; temperature ninety-nine and pulse became weak and rapid. Abdomen more distended but not tender. Dulness in flanks. Owing to patient's condition careful examination impossible.

December 25. Grew gradually weaker; vomiting continued. Died at 7.10 P.M. The young man's knees were the source of great interest to me. Our knowledge of syphilitic joint disease is not very full, and personally I have had little opportunity to study it. They are reported as filled with fluid when he entered the hospital. When I saw them the fluid had been absorbed in great measure. Motion was somewhat restricted, and they were *slightly* sensitive in one or two places, but on the whole one would scarcely suspect any lesion of the cartilage and there was nothing else about the legs at that time to attract attention. The pain in the legs of which he had previously complained had mostly passed away. The resemblance in the cartilages, as seen at the autopsy, to tuberculous disease was at first sight marked. It would have been very easy to have looked upon the lesions as a tubercular complication.

The desire to investigate that condition further led to making a transverse section just above the cartilage when the altered condition in the shaft showed itself, and led to still further investigation.

The death was comparatively sudden and unexpected. On December 20 he was preparing to go home in a few days, and through Dr. Drew, the house physician, I was trying to make arrangements with him to appear at my clinic, and allow me to lecture upon him. On the twenty-first his temperature shot up and a septic infection showed itself which within four days ended fatally.

This history falls far short of telling all the facts it would be pleasant to know, but on the whole it is interesting and fairly satisfactory. On the whole it is probable that few cases can be produced that are more complete from both clinical and pathological standpoints.

But one point was wanting, and that was the knowledge of disease in the parents.

After the young man was dead his father called upon Dr. Drew and told him that he wished to tell him that he had had syphilis before he was married; that it had always weighed upon his mind, and he wanted to tell of it in the hope that it might help the doctors in the interest which he saw they took in his boy's case. That so far as he knew the wife had never had any signs of disease, nor the children who had survived.

The sequence of a syphilitic child born at term who survived until early manhood, followed by two miscarriages, is extremely interesting. It suggests the possibility of some change in the mother's condition while carrying the first child.

Autopsy by Dr. Councilman, December 26, 1895, 11 A.M.

There is a slight general icterus. Both corneæ rather cloudy. The pupils of ordinary size. There are small, lenticular, dark discolorations, generally distributed on the posterior surface of the body, especially on the neck.

The scalp normal. Skull of ordinary thickness; dura not adherent. Pia normal. Brain and cord normal.

On the right side, over the lower ribs and immediately over the liver, the abdominal wall is tightly adherent. At one place where the abnominal wall is in contact with a large tumor mass on the surface of the liver, the muscle is infiltrated with a dense, white cicatricial tissue, which gradually passes into the surrounding muscular tissue. There is no caseation in the muscle. The anterior mediastinal glands are enlarged up to the size of two cm. in diameter. The glands at the upper end of the sternum are most affected. On section these glands are hard, of a yellowish color, and the greater part of some of the glands is filled with a dense yellow tissue resembling firm caseation.

The right lung free from adhesions. The entire lung somewhat edematous. In the posterior portion of the lung there are areas of lax consolidation, without apparent connection with the bronchi, and appearing more as edema than as inflammatory consolidation. The bronchi deeply injected and contain muco-purulent exudation. The left lung is adherent to a greater or less extent, and shows the same condition as in the right, but the lax consolidation is not so evident.

The heart of ordinary size; valves normal; ventricles not distended. Coronary arteries normal. The aorta is rather small and smooth throughout.

The larynx, pharynx and trachea normal. The mucous membrane of trachea somewhat injected.

In the peritoneal cavity is a large amount of purulent opaque exudation mixed with flakes of fibrin. The peritoneal surface of the intestine everywhere deeply injected, roughened and slightly adherent by flakes of fibrin which are found in various places on the surface. In the upper portion of the peritoneum there are numerous adhesions binding everything together.

The stomach, transverse colon, pancreas, duodenum and liver were tied up in adhesions. In these adhesions there are numerous solid caseous masses.

The vermiform appendix thickened, injected, turned backwards and upwards and adherent to the lower posterior surface of the cæcum.

The spleen tied up in masses of adhesions in the upper part of the abdominal cavity.

The liver intimately adherent to diaphragm. The entire surface of the liver, especially the right lobe is irregular, of a whitish color, the irregularity being due to large knobby projections with secondary projections on the surface of these. A deep depression almost completely separated the right from the left lobe of the liver. The wall of the gall bladder is thickened; the mucous membrane smooth. It contains a large amount of yellow bile.

A section through the liver shows dense masses of connective tissue in which there are small irregularly shaped caseous masses varying in consistency. In the left lobe of the liver in the vicinity of these cicatrices there are areas of slightly yellowish transparent tissue not sharply separated from the liver itself. The general color of the liver is yellow. Its tissue firm. All over the posterior and lower aspect of the liver there are dense irregular caseous areas which vary in consistency, of exceedingly irregular shape and surrounded by firm, dense, transparent, connective tissue. Where this tissue is most strongly developed no liver tissue is seen. The greatest mass of this cicatricial tissue was in the form of a

large tumor like projection in the vicinity of the gall bladder. This mass of tissue is directly adherent to the abdominal wall, and is continuous with the cicatricial tissue in this. The diaphragm is thickened, edematous, and filled with transparent, soft connective tissue. The gastro-hepatic lymph glands are enlarged, and on section show areas of caseation.

The spleen is enlarged and rather soft; on section homogeneous. Neither trabeculæ nor malpighian bodies are visible.

The pancreas in places, especially along its upper edge is infiltrated with rather transparent connective tissue which has in part substituted itself for the tissue of the pancreas. There are no definite caseous masses in this. The whole pancreas is firmer than normal.

Both kidneys are large; the surface hyperæmic; the capsule easily stripped off. On section cortex hyperæmic; pyramids pale; glomeruli appear prominent.

The stomach and intestines dilated. The wall of the stomach in the vicinity of the pilorus is thickened, due to the involvement of the muscular substance in the cicatricial tissue about it. The mucous membrane pale.

The small and large intestines normal. The mesentery is thickened, the surface hyperæmic, the glands enlarged; the enlarged glands are indurated, and, beginning necrosis, a few show at the periphery.

The mucous membrane of the bladder smooth. Prostate not enlarged. Seminal vesicles small, collapsed, filled with a transparent viscid fluid. Testicles of normal size. There is a slight thickening of the tunica albuginea at the hilus of each testicle with some masses of connective tissue. Substance of testicles denser than normal.

Examination of bone: Knee joint on right side was opened and examined. The synovial membrane somewhat injected, and here and there on the surface there are small papillary deeply injected masses of connective tissue. On either side of the condyles of the femur there is a slight erosion of the cartilage. Over the inner condyle there is a small smooth erosion with a deep depression of the cartilage extending inwards from this. All around the edge the cartilage is somewhat thinned.

Numerous sections were made through the bones of the lower extremities. The sections of the condyles of the right femur in places presents the normal appearance of the marrow. In other places, particularly well marked near one of the condyles, the bone has a yellowish, more fatty appearance. This does not involve the entire area of the bone, but extends more or less irregularly into the adjoining normal bone. In this yellowish tissue there is in one place an opaque yellowish mass in connection with the surface of the bone, and extending from a small depression in the cartilage. There are similar nodules of varying size found in almost every section made through the head. Many of these are surrounded by normal bone, and separated sharply from it. Others are surrounded by the pale, yellowish marrow. All of these masses are sharply circumscribed and of irregular outline. They have in general a distinct yellow color. No evidence of destruction of the bone is seen in or around them. They present the appearance as though masses of firm yellowish material had been pressed into the cancellated tissue. They are more yellowish and more transparent than tuberculous foci, and no smaller areas of extension are found near them. They vary in size from one-half to three or four cm. in their widest diameter. After sawing the head of the bone into thin sections it was split longitudinally, and similar small areas found in the shaft. In the left femur a similar condition is found. Between the condyles there is an area larger than any of the areas in the right femur and of the same color and general character. In the patella a small, circumscribed area is found. Sections of the heads and shafts of both tibæ show a similar condition to that of the femurs, but the nodules are less numerous. About several of the nodules the bone is intensely hyperæmic. The hyperæmia is especially marked in one of the nodules in the tibia. None of these nodules were surrounded by connective tissue, nor was there any increase of this in the bone. The bone itself does not appear to be altered in any way by the nodules; it is neither denser nor firmer, either in or around the masses. All of these masses were found in the bone, either in the head or shaft. There were none in the marrow, nor did any of them encroach upon this.

No similar masses were found in the bones of the head, in the sternum and in the vertebral column. It was not possible to examine the bones of the upper extremities.

Cover-slips from the peritoneal surface of the intestine showed many short chains of streptococci. Examination of all of the organs for amyloid gave negative results.

Cultures from the blood and from all the organs gave abundant pure cultures of streptococci.

Examination of the contents of the seminal vesicles showed sperma tazoa.

Anatomical Diagnosis: Syphilis, jaundice, atrophy of auditory nerves. Gummata and diffuse syphilitic cirrhosis of liver. Gummatous infiltration of abdominal wall, extending from the liver. Gummata and cicatricial contraction of pancreas. Induration of lymphatic glands with formation of gummata. Multiple gummata of the bones of lower extremities. Acute and chronic peritonitis. Acute hemorrhagic nephritis. Bronchitis, broncho-pneumonia and edema of lungs. Acute enlargement of spleen. General streptococcus infection.

Microscopic examination: The tissues for examination were hardened both in Zenker's fluid and in alcohol. The main interest in histological examinations centres in the bone on account of the unusual number of the lesions in this. Sections were made from the bone in various places involving the gummata and their vicinity, and the marrow of the bone at a distance from these. The bone was decalcified in 5 per cent. nitric acid and cut in celloidin. The sections were stained with hæmatoxylin and oesin, and with various aniline dyes. A singular feature of the bone lesions was that the gummata which were so prominent on the fresh sections of the bone were almost invisible after the bone had been in alcohol for several weeks. They could only be distinguished where the medullary spaces appeared to be filled up with a more solid material.

Sections through the marrow at a distance from the gummata show this to be rather more cellular than the ordinary fat marrow. In places the cells are so abundant that they fill up the entire space. These cells are composed of large marrow cells, giant cells and leucocytes. In the number and

character of the cells in some places the marrow simulates that of myelogeneous leucæmia. No examination of the blood was made during life. The examination of the sections of the blood vessels in other organs shows the absence of leucæmia.

Sections stained for bacteria showed numerous streptococci in the large vessels of the marrow, both in clumps and in single chains. After staining, the gummata in the sections are sharply circumscribed and are surrounded by an area, in which, to the naked eye, the bone appeared paler than normal. The central portion of the gumma is composed of a dense tissue which passes at the periphery into a well marked reticulum and which contained no normally staining cells. In some of the sections there are numerous giant cells with mural nuclei. These giant cells are generally found in the centre of a smaller and denser mass of the tissue, and are in no way connected with the trabeculæ of bone. Outside of this denser tissue the marrow is substituted by a pale mucoid looking tissue, containing small masses of the same tissue as that composing the central mass. In this tissue are here and there small areas of cells of the same character as those in the marrow. With a high power the central mass is composed of dense cicatricial tissue, forming a more or less definite reticulum and enclosing small, round, spindle-shaped, or indistinctly staining cells. In but a few places is there any nuclear detritis. Both cells and tissue seem to undergo a slow necrosis. The chromatin of the nucleus gradually losing its power of staining, although in the densest part of the tissue, the nuclei were still faintly visible. The vessels in this could still be recognized as such. The walls are thickened, refractive, and the reticular cicatricial tissue is connected with them. No blood corpuscles were found in them. At the edge of the dense masses the tissue is distinctly reticular. The meshes of this are exceedingly irregular and formed of refractive, wavy, more or less ragged masses of fibrillæ. The density of the reticulum varies. In places the fibres forming it are so broad and refractive, and the enclosed spaces so narrow, that it simulates canalized fibrin. In places large glanular masses, with a nucleus similar to that of the polynuclear leucocyte are found in the

reticulum. There are numerous blood vessels in this. In the periphery they contain blood corpuscles, and the walls appear normal. Elsewhere the walls are thickened and the vessels appear to be converted into the same dense refractive tissue as the reticulum. On the outside of the paler tissue there is a great deal of fibrin and hemorrhage. The bone trabeculæ in all parts of the tissue are not altered in form. The bone corpuscles within them do not stain, and here and there fractures extending into them are seen. There are neither osteoclasts nor osteoblasts in connection with them. The necrosis of the bone corpuscles extends well into the trabeculæ in the paler surrounding tissue.

Kidney: the tissues were hardened in both Zenker and alcohol. The Zenker preparations give the best results. There is intense congestion of the entire cortex. The epithelium is swollen, very granular, and in places almost fills the lumen of the tubules. In some places, comprising either single cells or entire sections of tubules, the swollen cells have a loose, reticular looking protoplasm. In other places there is extensive necrosis of the epithelium, the nuclei being converted into shrunken, solidly staining masses, and some not staining at all. In a great number of tubules, usually in definite areas, there are blood corpuscles, either perfectly pure or mingled with more or less granular material. Almost all of the glomeruli are altered. The cells in them are increased in number, they are swollen, and the vessels are obliterated. In spite of the vascularity of the cortex, in only a few of the glomeruli are any blood corpuscles found. In the entire kidney the intertubular tissue is increased, and contains a varying number of cells. In some places, especially in the cortex and in the intermediate zone of the kidney, there are masses of cells of the same character as those found in acute interstitial nephritis. These cells are large, with very granular protoplasm, and a reticular nucleus. In other places there are collections of distinctly lymphoid cells. In addition to the red blood corpuscles in some of the tubules of the pyramids, there are distinct hyaline casts. Fibrin is also found in the tubules.

Sections of the lung show intense congestion, with some atelectasis and hæmorrhage. One of the sections passes

through an area of broncho pneumonia, and in a few of the bronchi there are masses of leucocytes.

Liver: sections of the liver were hardened in Zenker and alcohol.

Sections were made involving the gummata, the surrounding tissue, and the apparently intact tissue of the liver. There is everywhere in the liver a very diffuse formation of connective tissue, which is in places more marked than in others. This connective tissue formation is not at all interlobular in character; it extends throughout the tissue along the capillaries, many of which are obliterated. The liver cells are small, irregular, and often broken from their connection with one another.

In the gummata there could be recognized a central and peripheral mass. The central mass was sharply circumscribed. It is composed of a dense tissue, very similar to that forming the gummata of the bone. No nuclear detritis could be made out of it. In the periphery of this there was a dense cicatricial tissue extending into the surrounding liver substance and connected with the interstitial tissue in this. In places small masses of broken down liver cells were enclosed in this. Where the tissue adjoins the liver, rows of atrophied liver cells, simulating bile ducts, are found. While this is the general character of the gummatous tissue, in other places it appears to be formed by necrosis of the cirrhotic liver tissue. Here it is much looser, more granular and remains of liver cells can be found in it. Numerous masses of bacteria were found in the liver capillaries.

Sections of the pancreas showed large masses of connective tissue in the septa and a slight general increase in the connective tissue throughout the gland. In the vicinity of the larger masses there is an ingrowth of the connective tissue between the alveoli and in these places there are aggregations of round cells. In the places of the most marked interstitial increase the cells of the pancreas are small and atrophic. Several of the large vessels in the interstitial tissue are filled with leucocytes.

Sections of the muscle of the abdominal wall adjoining the liver gummata show an extensive formation of connective tissue between the bands of the muscular fibres, in places

entirely substituting itself for this. The connective tissue is loose and reticular containing very few cells. In a few places it is dense and homogeneous, containing no cells. The blood vessels are congested and there are numerous hemorrhages in the tissue. Many of these hemorrhages appear to be in connection with blood vessels containing masses of bacteria. Some of the vessels are thrombosed.

Microscopic examination of various lymphatic glands shows about the same condition in each. The blood vessels are deeply injected. The lymph sinuses dilated and filled with leucocytes and epitheloid cells. Many of the vessels in the glands contain masses of bacteria. In some of them there is a stroma of connective tissue extending diffusely through the gland. Giant cells are occasionally found in these glands.

This case is interesting anatomically from the extension and character of the syphilitic lesions the absence of amyloid infiltration, and the absence or slight character of the testicular lesions. Chiari has described a number of cases of gummatous osteomyelitis in the long bones. All of his cases were from acquired syphilis, and the character of the lesions, so far as it is possible to tell from the histological descriptions, very different from those in this case. The bone lesions here differ from any other descriptions of bone gummata, and from the gummatous processes in other organs. On account of their rarity and the difficulties attending the histological examination there exists nothing but the most general descriptions of the histology of the lesions in bone syphilis. The chief peculiarity which distinguishes these bone lesions from gummatous processes elsewhere is the absence of reactive inflammation, shown by cellular infiltration and connective tissue formation, in their vicinity. The process appears to be one of necrosis with the conversion of the marrow into a loose reticular mucoid-like tissue. The necrosis of the bone trabeculæ was not marked by a sharp boundary. When a trabecula extended from the surrounding tissue into the gumma the normal bone cells seemed gradually to become necrotic. The blood vessels were occluded and their walls took part in the formation of the reticulum, but there was nothing to indicate that the vascular lesions were primary.

In the liver also the process was different from that generally found. Here the process was characterized by the diffuse character and extent of the lesions.

An accompanying streptococcus infection is so common in death from visceral syphilis that it may almost be regarded as a part of the syphilitic process. In most cases there are no accompanying acute lesions which may be referred to this. In the present case the acute peritonitis should be regarded as caused by this organism, and the acute nephritis was probably due to the absorption of the chemical products produced by the cocci.

XVIII.

TWO CASES OF AMŒBIC ENTERITIS.

By Lawrence Watson Strong, M.D.,
Second Assistant in Pathology, Boston City Hospital.

While amœbic dysentery is a comparatively rare disease in this locality yet endemic sporadic cases occur with no suspicion of an introduction from any region known to be infected. As such cases may be overlooked on account of their rarity and especially if their clinical symptoms are at all atypical, it may be of interest to report two cases, both apparently endemic, and with unusual clinical symptoms.

It seems, moreover, very probable that even if the typical form of amœbic dysentery is rare in the north, yet the amœba coli may occur in our soils and waters.

Amœbic dysentery is also known as tropical dysentery, and with some reason, as it is far more prevalent in the tropics and subtropics, but it may occur more or less through the United States and middle and northern Europe, even as far north as St. Petersburg.

For this reason the term amœbic dysentery is preferable to tropical dysentery and more especially as all cases of dysentery occurring in the tropics are not of amœbic origin.

Both the following cases occurred in this hospital within the past year. As one case was not a colitis and had no diarrhœa it is not to be described as amœbic dysentery, but from its unusual clinical and pathological conditions it is of even greater interest, as showing the possibility of unrecognized amœbic invasions.

Case I. — ——— ———, aged sixty-four, married, born in Ireland and a tailor by trade, has lived in the vicinity of Boston, and has never been south as far as can be ascertained. Has always been well until four years ago when he had influenza. Since then he has been suspicious of his

friends, has lived apart from his family and has had some delusions of persecution. Little else is known of his previous history, and his statements in regard to himself are considered unreliable. He says that he has had several attacks of an illness resembling the present in the past four years. In the middle of July, 1897, patient began to complain of abdominal pain: this was followed by severe diarrhœa and some vomiting, succeeded in turn by obstinate constipation. For a week he kept about, although it was evident to his landlady that he was getting weak, and at the end of this time he was found by the police lying in the street in an exhausted condition. He entered the hospital July 28, 1897.

Physical examination showed a fairly well-nourished man, greatly exhausted; pulse weak and irregular. Heart normal; a friction rub at base of right lung. In the epigastric and right hypochondriac regions was a large tense tumor, tender on palpation. Slight general abdominal distension.

The patient received stimulant treatment, but he gradually grew weaker, and died July 30, 1897.

Post-mortem examination July 30, 1897: Body of an elderly man, age sixty-five to seventy years. Fairly well built and nourished. Abdomen distended.

Peritoneal cavity: old adhesions between omentum and anterior wall of abdomen, above which was considerable thick yellow pus, especially over surface of liver, the border of which was low. Transverse colon and omentum were adherent to inferior surface of liver, on the anterior surface of which, near the inferior border and below the falciform ligament was a white area surrounding a cavity from which pus escaped. From 200 to 300 cc. of thick, yellow, slimy pus, turbid, with yellow and grayish flecks were contained in the peritoneal cavity. A cover-slip of this showed a few pneumococci.

Under surface of diaphragm showed marked peritonitis, with thick soft fibrinous layer on surface.

Intestines a little injected, somewhat inflated, contained considerable fluid contents. At cæcum and extending up for some distance were hard fæces.

Appendix normal, small, old adhesions extended from cæcum to abdominal wall. Stomach and small intestine

normal. In the cæcum surrounding the opening of the appendix was an area 3 cm. in diameter, covered by loose shreds of tissue; surrounding this was a zone 1 cm. in breadth, shreddy, yellowish and elevated. In the vicinity there were a number of superficial, shreddy, yellowish ulcers, varying from 2 to 10 mm. in longest diameter, and surrounded by a reddish border. Ilio-cæcal valve was involved to some extent.

The liver contained four abscesses, the largest 12 by 9.5 cm. in diameter, in the upper part of right lobe, extending into the left, connected with an abscess in the spigelian lobe, which was red and fluctuating on the surface. This second abscess was the size of an orange, and was between the gall-bladder and the suspensory ligament. The third abscess was to the right of the gall-bladder, and had ruptured into the peritoneal cavity. The fourth abscess was much smaller, and close to the ruptured one.

These abscesses had a hemorrhagic, worm-eaten wall, composed of liver-tissue, and were filled with thick, yellowish-gray pus.

With the exception of a slight arterio-sclerosis the other organs were normal. The anatomical diagnosis was chronic and acute amœbic ulcerations of cæcum, amœbic abscesses of liver and acute peritonitis. Cultures from the peritonaeum and liver showed pneumococcus. Other organs negative.

Microscopic examination: Section of the colon in the region of the appendix showed the characteristic ulcers of amœbic dysentery, described by Councilman and Lafleur. The ulcers varied in depth, had ragged and undermined edges, with marked thickening of the submucosa and infiltration with pus-cells. The submucous coat was first and most affected, and the ulcers were formed by its gradual infiltration and softening, with subsequent necrosis of the overlying mucous membrane. The amœbæ were most numerous at the edges of the ulcer, where twenty or more were often seen in a single field with the low power. They were found less abundantly as the distance from the ulcer increased, until finally they occurred singly in otherwise normal submucous tissue. A few were found in the mucous membrane. Around the circumference of the ulcer was a zone of pus formation,

but as the distance increased the pus-cells disappeared and lymphoid cells took their place.

Sections in various places through the liver showed typical amœbic abscesses without any definite wall. The liver-tissue passed gradually into the abscess, but the margin was very irregular, some portions of the liver-tissue resisting the action of the amœbæ more than others. Sometimes liver-cells, with stained nuclei, were in contact with the abscess contents; sometimes they were separated from it by a considerable area of necrotic tissue. Amœbæ were found fairly abundant, for the most part in the wall of the abscess or the liver substance immediately adjoining, but not free in the lobules. Outside of the abscess there was extensive necrosis of the liver-cells, some of which were vacuolated and without nuclear stain. Masses of liver-cells were broken away from the lobules and lay surrounded by connective tissue and capillaries. There was diffuse infiltration with lymphoid cells.

While the general characteristics of the intestinal ulcers were the same as those described by Councilman and Lafleur, it is to be noted that in this case they occurred in the region of the ileo-cæcal valve and not in the transverse or descending colon. This has some significance as showing that the means of infection of the liver was probably not by the abdominal cavity direct, but by the blood stream or lymphatics, although the seat of the abscesses in the liver was the usual one, that is, the right lobe adjacent to the hepatic flexure where direct infection might have been expected. It is also noteworthy that the ulcers were more superficial than most of those in Councilman's and Lafleur's cases, not passing through the submucosa, and this again makes it unlikely that the amœbæ passed into the peritoneal cavity. The fact that the intestinal lesions were slight in depth and number in comparison to the size and number of the abscesses in the liver would signify that there was an early invasion of the circulation.

Case II. — ——— ———, age, three, born and lived in Boston. Well until six months before he came under observation, when he began to complain of pain in abdomen and to be fretful. There is no history of diarrhœa, and the most that can be said is that he appeared irritable and seemed to have

some trouble in the abdomen. In March, 1897, he had a severe attack of bronchitis, with swelling of cervical lymph glands. May 22, 1897, he had a sore throat and was admitted to South Department of the Boston City Hospital, May 24, for diphtheria with laryngeal stenosis. Was intubed without relief and died the following day.

Post-mortem examination May 25, 1897: Well developed and nourished child, with lesions of tonsils, larynx and trachea characteristic of diphtheria. There were enlarged tubercular mesenteric lymph glands, with some caseation.

In addition to general hyperplasia of the intestinal lymphatics due to diphtheria, there was a large, prominent Peyer's patch just above the ileo-cæcal valve, containing two ulcerations. The larger, 1½ cm. in diameter, was ragged with raised and undermined edges. Its base was ragged and covered by necrotic caseous material. The smaller, 5 mm. in diameter, was more regular, but had a similar ragged, necrotic base.

The liver showed few miliary tubercles. Other organs showed no lesions of significance.

Anatomical diagnosis. Diphtheria: chronic tuberculosis of mesenteric glands and tubercular ulcers of intestine. Cultures showed Klebs Lœffler bacilli in the throat and lungs, and streptococcus in lungs, heart and kidney. Other organs sterile.

Microscopical examination: At the edge of the Peyer's patch mentioned in the gross description, and which contained numerous miliary tubercles, was a space covered over by a mucous membrane, representing an undermined cavity. The edge of this space was lined with tuberculous tissue, and in an adjoining miliary tubercle just at the edge of the caseation were several perfectly typical amœbæ.

Another section of the small intestine showed numerous amœbæ in the submucosa along the outer edge of tuberculous foci, and actually in the tuberculous tissue. These amœbæ were perfectly characteristic in their form, in the shape of their nuclei and in their manner of staining; amœbæ were also found in other places in the submucosa surrrounded by lymphoid cells, and with no change in the tissue around them.

The tubercular ulcers elsewhere did not show them. Sections of the large intestine show numerous enlarged follicles, several of them with necrotic centres, but no amœbæ were found in these places.

The infection here is interesting in being a combination of tuberculosis, diphtheria and of amœbæ. The necrosis of the centres of the follicles without the formation of tuberculous tissue are possibly a part of the diphtheritic process, although the agency of tuberculosis and amœbæ cannot be excluded. It is especially interesting to find amœbæ in the small, instead of the large intestine.

The recognition of the amœba in the first case was greatly facilitated by the use of Mallory's differential stain with thionin, and indeed it would have been impossible to have identified them in the liver without this stain, while with it they come out very clearly.

Since the presence of amœbæ was demonstrated not only in the stools of patients suffering with dysentery, but also in the intestinal lesions and in the abscesses of the liver of such cases, attempts have been made to reproduce similar conditions by injecting animals with dysenteric stools or cultures from these.

The most recent investigators, Janowski and Boas, in Germany, are as yet unwilling to admit that the casual relation between the amœba coli and dysentery is proved, first, because they have been unable to find the amœba in all cases of tropical dysentery, and second, because they have not been successful in reproducing the disease by inoculation.

That they have been unable to find the amœba in all cases of tropical dysentery does not affect its etiological significance at all, inasmuch as there certainly are forms of dysentery in the tropics which differ from the picture presented by amœbic dysentery which may have another etiological factor.

In his study of dysentery, Janowski has endeavored to classify the various kinds as epidemic and endemic, of which the first is bacterial and the second is amœbic.

The dysenteries of bacterial origin do not concern us directly, but it is sufficiently proved that there is no specific organism which is the cause of all. Janowski asserts that a

symbiosis of various bacteria as streptococci, staphylococci and colon bacilli is important in their production. That there is a distinct affection in which the amœba coli is invariably present and is the essential factor is undeniable, though the complete biological proof has not yet been established.

The main evidence that the amœba should be considered as a casual factor is that cases of dysentery in which amœbæ are found conform both clinically and anatomically to a definite type of disease which differs from those forms of dysentery in which amœbæ are not found.

The theory has been advanced that the etiology is a double one, produced by symbiosis between the amœba coli and various bacteria. Whether symbiosis with bacteria has an influence or not is an interesting problem, but it does not affect the etiology. It is the amœba alone which produces the lesions.

There has been a great amount of work done in attempting to reproduce dysentery by injection of amœbic stools and cultures into the rectum of dogs and cats. These experiments have had a varying degree of success, but must be set aside as imperfect, and no conclusions drawn from them because the stools and cultures used were impure.

It has been a matter of great difficulty to obtain cultures of amœbæ free from bacteria, and until recently there has been no scientific classification based on morphology and development. Classifications previously made have not been upon morphological differences, but rather on pathogenic properties.

Thus Quincke and Roos, whose classification has been largely used, described three forms of amœbæ found in man: 1, amœba coli (Lösch) or a. dysenteriæ (Councilman and Lafleur), producing dysentery in cats; 2, amœba coli mitis, non-pathogenic for cats; 3, amœba coli vulgaris found in healthy individuals.

This classification is not complete, nor is it proved that the differences are absolute and invariable, and a better classification based on the morphology and development should take its place.

Various investigators have found amœbæ in the stools of other diseases, and even in those of healthy individuals and in healthy animals.

Celli and Fiocca found amœbæ in the intestines of frogs, fowl, sheep, guinea-pigs and cats. They also found amœbæ in the genitalia of women. Out of seventy-eight examinations of the stools of children they found various amœbæ in twenty-six cases (fourteen healthy children, fifty cases of intestinal catarrh, five of green diarrhœa, six of dysentery, and three of follicular catarrh). In two cases amœbæ coli were found. Out of forty-six examinations of adults amœba were found in one healthy individual. These results show that amœbæ occur more frequently in children than in adults.

Quincke and Roos found amœbæ in the stools of healthy men after the administration of Carlsbad salts. Cunningham and Lewis found amœbæ in the stools of eighteen per cent. of cholera patients examined, and amœbæ have also been found in cases of typhoid fever. Boas, on the other hand, examined forty-three normal individuals, and many cases of chronic diarrhœa without finding amœbæ. It is to be noted that the amœbæ found are not known to be amœbæ coli; indeed, it is probable that for the most part they were not of that variety, though we cannot speak with certainty on this point as they were not studied.

As to the presence of the amœba coli in healthy individuals the case is not different from the occurrence of the pneumococcus in the throats of people who have not pneumonia.

Summing up the result of the examination of the stools of healthy individuals and of the various diseases studied, it is evident that the mere presence of amœbæ in the stools is not sufficient for a diagnosis of amœbic dysentery, but when in a case with the characteristic clinical picture they occur in large numbers there can be no question of the relationship

That there may be other varieties of dysentery due to other amœbæ is quite possible, and indeed another organism has been cultivated from certain cases of dysentery.

The only satisfactory work in growing, describing and classifying amœbæ has recently been done by Celli and

Fiocca, who found that amœbæ would grow abundantly on fucus crispus, a sea alga, and best on a five per cent. alkalinized solution in water or bouillon. On this medium it is not difficult to procure cultures with a slight admixture of bacteria. A culture, absolutely free from bacteria, was exceedingly hard to obtain, and would not live more than a few days even after repeated transplantations. From this circumstance they argue that symbiosis with bacteria is essential to their life.

According to these authors, though it is difficult to procure a culture free from bacteria it is comparatively easy to separate the varieties of amœbæ from each other, because their differences in the encysted state are marked, and they can then be isolated by the platinum needle; moreover, the various amœbæ grow exclusively in certain localities, and cultures from each source will reveal but a single variety.

A third method of separating them is by taking advantage of the fact that one species outgrows another, or requires a shorter period for its cycle of evolution.

In describing amœbæ they note the locality where found, the form, motion, size and structure in the amoeboid in the resting and the encysted states, and the length of the whole cycle of evolution.

Amœbæ are found in cultivated soil to a depth of two metres, and in altitudes as high as 5,000 feet. They are found alike in water and soil, and they may even be found in the air.

A temperature of 50 degrees C. kills amœbæ within an hour if they are in the amœboid state. The encysted forms live even at a temperature of 55 degrees C. for four days.

Without access to the air growth does not take place, though the ambœbæ may live in the encysted state for several months. They are much more sensitive to the action of antiseptics than are bacteria; they cannot grow on an acid medium.

Celli and Fiocca recognize by their classification amœba lobosa, with subvarieties of guttulata, oblonga, undulans and amœba coli; and second, amœba spinosa with varieties diaphana, vermicularis and reticularis.

Amœba coli is further described as follows: Locality from which obtained; water from the Nile canal; earth in neighborhood of dysenteric feces and elsewhere.

In the amœboid state the amœba coli has a lobular form (lobose type) in which it sends out numerous, lobular hyaline pseudopodia. Its size varies from 10–30 μ. In structure it possesses uniform entoplasm and a slight hyaline ectoplasm, a vesicular nucleus which sometimes contains a vacuole.

In the resting state the amœba coli has a simple contour, a uniform finely granular protoplasm, and its size varies from 1.5 to 2 μ. There are abundant degenerate forms with granules in the centre which have been erroneously considered to be spores of the amœbæ.

In the encysted state the amœba coli has a double contour, the inner is thicker than the outer, and the contents of the cyst are finely granular.

The cycle of development has the following characteristics: In from twelve to fifteen hours the amœba emerges from the encysted state and assumes the amœboid form. After forty to forty-eight hours most of the amœbæ are in the resting state, while at the end of sixty to sixty-five hours they are again encysted or else degenerate.

It remains to be seen whether the disease can be reproduced by inoculation experiments upon animals of cultures of amœba coli free from bacteria. Such experiments may very possibly be unsuccessful, perhaps from a lack of susceptibility of the animals used, perhaps from lack of proper conditions, for amœbic growth in a normal intestine. The association with certain bacteria which may aid in the development of their pathogenic powers may be necessary. But whether or not a complete biological proof is established the facts cited by the German observers, Janowski and Boas, are not sufficient to overthrow the already-established relationship between amœba coli and a certain type of dysentery.

The second case has its main interest in showing the possibility of the infection with amœbæ of a lesion produced by other conditions. That they did not produce their characteristic lesions may be due to a very recent infection, or to the fact that previous infection in some way interfered with the development of their pathogenic properties.

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XIX.

A REPORT OF A CASE OF APPENDICITIS, SHOWING THE RELATION OF THE COLON BACILLUS AND THE STREPTOCOCCUS PYOGENES AS ETIOLOGICAL FACTORS.

From the Pathological Laboratory of the Boston City Hospital.

By Joseph J. Curry, M.D.,
Assistant in Pathology, Harvard University Medical School.

R. C., a young man, a travelling salesman, aged twenty-one, entered the Boston City Hospital in the service of Dr. Lovett, August 24, 1897, with the following history:

EXTRACT FROM CLINICAL RECORDS.

Family history. — Negative.

Past history. — No previous attacks; has always been more or less constipated. Habits good.

Present illness. — Began vomiting three days ago; had pain in pit of stomach, considerable soreness in this region. Vomiting was frequent on the first day, diminished on second; pain kept severe: was obliged to go to bed yesterday. Symptoms became more severe and patient was sent to the hospital.

Physical examination showed the young man to be well developed and nourished; heart and lungs negative; pulse, 120, of fair strength; general tenderness over abdomen; no tumor.

Ether and operation by Dr. E. W. Dwight; a two and one-half inch incision made at McBurney's point.

On opening abdominal cavity a moderate quantity of seropurulent foul-smelling fluid escaped. Appendix was one and one-half inches in diameter, swollen, inflamed and buried in a mass of inflammatory exudate. There were numerous adhesions of omentum to the mass.

The appendix was removed, the abdominal cavity washed out with sterile salt solution, and iodoform gauze placed in opening for drainage.

Patient improved very slowly for two weeks after operation. At this time there was still considerable discharge from wound and some general abdominal tenderness. From this time the patient's condition became gradually worse. Six days later, or twenty days after operation, patient vomited considerably; abdomen became swollen. These symptoms became rapidly more severe, and he died the following day — three weeks from time of operation. The last day fecal matter was discharged through the opening. No autopsy.

Bacteriological examination. — Cultures were taken at time of operation from the exudate about appendix, also cover-glass preparations. The cover-glass preparations upon examination showed few pus cells, considerable granular detritis, and numerous stout bacilli.

Cultures (Lœffler's blood serum-slants) showed numerous colon bacilli and a liquifying bacillus. *No* streptococci or staphylococci.

Macroscopic examination of appendix showed a sausage-shaped mass, about 7 cm. long and 3 cm. in diameter. On section showed a sloughing mucous membrane, covered with a reddish gray exudate. Wall of appendix about 1 cm. in thickness, and made up chiefly of fat and inflammatory tissue.

Anatomical diagnosis: acute appendicitis, with inflammation of surrounding fat tissues.

Microscopic examination. — "Sections of the appendix were made in various places. The least altered portion shows necrosis of the mucous membrane, with rather superficial erosion. There is swelling of the lymphoid follicles and slight infiltration with leucocytes. The peritoneal coat over this is swollen, filled with hemorrhage and infiltrated with leucocytes. All the vessels are greatly dilated. At other places the sections show a total necrosis of the mucous membrane, extensive purulent infiltration of the submucous tissue, extending directly through to the peritoneum. The peritoneum is thickened and infiltrated with leucocytes. In places where the purulent infiltration is less evident, and in

the adjoining mesentery there is enormous proliferation of connective tissue cells. At various places in the tissue there is extensive hemorrhage and more or less fibrin."

The above descriptions, macroscopical and microscopical, were made by Professor Councilman.

Sections of the appendix, at the point showing necrosis of the mucous membrane and purulent infiltration of submucous tissue, were stained for bacteria by the Methylene-Blue method and by the Gram-Weigert method. In the first instance Unna's Alkaline Methylene-Blue solution was used and the staining done after the method described by Mallory.[1] By this method bacteria, which decolorize after Gram, are stained.

Sections stained by this method showed numerous moderate-sized bacilli, resembling the colon bacillus. These bacilli were not only numerous on surface of necrosed mucous membrane but were seen in large numbers in the submucous tissue, and in the surrounding inflamed fat tissue. The bacilli were so numerous that no other organisms could be made out definitely.

By Gram-Weigert method the colon bacilli are decolorized. Sections stained after this method showed *many* typical chains of streptococci in and beneath the necrotic mucous membrane. Streptococci were also seen in less numbers in the submucous tissue, and in the surrounding fat tissue. There was a small number of rather large bacilli seen in the necrotic mucous membrane which stained after Gram.

It will be seen that the streptococci were absent both in the cultures and in the cover slip preparations which were made from the exudate. In the cultures we find the colon bacillus and a liquefying bacillus, the colon bacillus in a profuse growth, the liquefying bacillus in small numbers. This latter was in all probability accidental, and not an important factor in the inflammation.

Upon examining sections stained after Gram we find numerous streptococci in the inflamed tissue. The colon bacilli by this method being rendered invisible, the streptococci stand out prominently.

This is a most important point. There have been many investigations and reports on the bacteriology of appendicitis.

In all these reports the colon bacillus has occurred alone or combined with various non-pathogenic bacteria in the great majority of cases, and in only a comparatively small percentage of cases was it combined with the streptococcus or other bacteria ordinarily found in acute inflammatory processes. In fifty cases occurring in this hospital reported by the writer in the [2] Medical and Surgical Reports of the Boston City Hospital 1897, the colon bacillus occurred in 46 cases or 92 per cent. In 20 cases or 40 per cent. the colon bacillus occurred alone, while the streptococcus occurred in pure culture in but 1 or 2 per cent. The streptococcus occurred in 15 or in 30 per cent. of the total number, while the staphylococcus aureus occurred once. In the mixed cultures the streptococcus occurred once with the staphylococcus aureus, and thirteen times with the colon bacillus. The percentage of cases in which the streptococcus was found in these cases is rather higher than has been reported by most other observers. In twenty cases [3] Achard and Broca found it in the same percentage (in six cases). [4] Osler mentions the observations of Hodenpyl on this subject. He found in sixty-one cases the colon bacillus in fifty-seven. In these fifty-seven cases it occurred alone in fifty. There have been many other reports made by different observers which agree very closely with the above quoted: thus, in 1893, [5] Hodenpyl in eleven cases, found the colon bacillus in pure culture in ten cases, and once the colon combined with the streptococcus. He reported with these twenty-four cases of other investigators. In these thirty-five cases the colon bacillus occurred in pure culture in thirty-two.

The writer in his report of last year tried to account for this high percentage of cases of appendicitis, *apparently* due to the colon bacillus by the theory that the colon bacillus, which is practically always present in large numbers in the severer inflammations of the appendix and always in cases of perforation, prevented the primary organism from developing on the culture media. [6] Welch's opinion supports this view, and was quoted by the writer. He says: "There is reason to believe that the highly resistant colon bacillus may survive in an inflamed part after the primary organism which started the trouble has died out or has been crowded out by the invader." This view is also held by [3] Achard and Broca who

say: "It is probable that in appendicitis, as in other cases of suppuration, the colon bacillus is aided by other bacteria, while it does not wait long before it outnumbers and destroys them." In support of this view the writer referred to three cases, in which at the primary operation, no streptococci were present, but were subsequently found; twice at secondary operations and once at autopsy. There was only one objection that could be made to drawing the conclusion that the streptococcus was the primary factor. This was that it could not be *absolutely* ruled out, that it was not introduced at time of primary operation. After nearly a year's study of this subject it occurred to the writer that examination of sections stained by the Gram-Weigert method would help solve the difficulty. This is the first case in which it was applied. We have here a case in which no streptococci were found after careful examinations, both by culture and coverslip, at time of operation, but in which the streptococci were found in sections of the appendix. In this case there was no opportunity for any doubt that it was the primary organism and no possible chance of it having been introduced at time of operation. The appendix was placed immediately after removal in 80 per cent. alcohol and sent to the pathologist for examination.

Further investigations of a large number of cases are necessary before we can draw definite conclusions. The writer suggests that all cases be studied by sections of appendix stained after Gram as well as by cultures and coverslips. This latter is of great value in connection with cultures. It quite frequently happens that the streptococci may appear on coverslip preparations and not in cultures, for the reason mentioned above, namely, colon or other bacteria in large numbers inhibiting its growth. The coverslip preparations may also be stained by the Gram method to remove the colon bacilli, and thereby render it possible to recognize the streptococcus, if present, even in small numbers, easily.

The bacteriological study of appendicitis has been very unsatisfactory in the past. The writer believes that systematic examinations by the methods above referred to will throw light on the etiology of appendicitis, and place the colon bacillus in a minor position as an etiological factor.

References.

1. Pathological Technique, Boston, 1897, Mallory and Wright, pp. 246 and 270.
2. Boston City Hospital Medical and Surgical Reports, 8th series.
3. Gaz. Heb. de Méd et de Chir., April 1, 1897.
4. Osler's Practice of Medicine, p. 432, 1897 edition.
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XX.

THE NEW SURGICAL SERVICES.

By Herbert L. Burrell, M.D.

In the year 1897 there went into effect a new plan of conducting the work in the surgical services of the hospital.

For a number of years it has been recognized that the system under which the surgical services were conducted was open to many objections. The custom prevailed of a surgeon having four months of service and the remainder of the year he was not actively connected with the hospital.

This system was supposed to possess advantages in that every four months it brought a new surgeon in charge of cases who might see conditions in the patients that had been overlooked by his predecessor.

Again, it was a system that was devised to accommodate surgeons who, from force of circumstances, were able to give only four months of their time to the hospital.

The disadvantages of the system were that it made divided responsibility, for every four months the patients (from seventy to eighty on each of the surgical services) passed into another surgeon's care. In the course of events it required from a fortnight to a month for the new surgeon to thoroughly understand the condition of the patients. It required from a fortnight to six weeks for the service to be conducted according to the ideas of the new surgeon.

Again, the last month of service was more or less conducted as a preparation, in sending patients out, for the advent of the next surgeon.

The same character and quantity of work was demanded of a surgeon after twenty-five years' connection with the hospital as when he first became visiting surgeon. This was obviously an error, for as men grow older they have less capacity for hard physical work, but become very valuable as

a result of their accumulated experience and mature judgment.

Again, surgeons to out-patients, in the course of events, frequently served in that capacity, doing so-termed "Minor Surgery," for from five to fifteen years, so that many surgeons to out-patients were forty years of age before they were given the full responsibility of an active house service. When that responsibility came to them it was not given gradually, but was suddenly presented to them by the death or resignation of one of the surgeons.

The technique of modern surgical work is such that it requires constant practice, and it was generally recognized by the surgeons of the hospital that if a feasible plan could be provided to diminish the amount of work in a given length of time, and to distribute it more evenly throughout the year, it would be desirable.

All of these circumstances had led to a serious consideration for a number of years of the methods of doing surgical hospital work. The following rules were adopted by the Board of Trustees and are now in effect:

Senior and advisory surgeons shall have performed active service in the surgical department of the hospital for a period of at least fifteen years. They shall be members of the visiting staff. They shall have no regular terms of service, but may be called upon at all times for consultation and advice by the visiting staff of the hospital.

The senior surgeons shall have the same privileges as to the care of patients as senior visiting surgeons.

Each of the three surgical services shall, as far as possible, be equal to the other services in respect to the number of beds and the character of the cases; and the cases shall, so far as practicable, be assigned in regular rotation to the different services. Each service, both house and out-patient, shall have a senior visiting surgeon, a junior visiting surgeon, a first assistant visiting surgeon, a second assistant visiting surgeon and a third assistant visiting surgeon.

The senior visiting surgeon shall have the general direction of his service during the entire year. He shall be on active duty four months. When on duty he shall have the assistance of one or more of the assistant visiting surgeons

belonging to the service, in case he desires it. He shall take full charge of such cases as he wishes, and may assign such of his work to the assistant visiting surgeons as he sees fit. He shall also have the right to take entire charge of such cases as he desires, when not on active duty, and for such time as he wishes.

The junior visiting surgeon shall be on active duty four months. When on duty he shall have full charge of the wards, being responsible, however, to the senior visiting surgeon. He shall take full charge of such cases as he wishes, and may assign such of his work to the assistant visiting surgeons as he sees fit, having, when on active duty, the same privileges in respect to the services of the assistant visiting surgeons as the senior visiting surgeon enjoys when he is on duty. He shall also have the general direction of the service when the senior visiting surgeon from absence, illness or other reasons, is unable to perform his duty.

The first assistant visiting surgeon shall carry out the direction of his senior on the service, both in the wards and in the out-patient department. His special service shall be in the hospital wards. When on duty he shall have full charge of the wards, being responsible, however, to the senior visiting surgeon in his service. He shall have the same privileges in respect to the service of the other assistant visiting surgeons in his service, which his seniors have when on duty.

The second assistant visiting surgeon shall be on duty in the out-patient department during the regular months assigned to him, and during those months, as well as the rest of the year, his services shall be at the disposal of his seniors, and he shall have charge of the wards during such time as his seniors shall direct.

The third assistant visiting surgeon shall perform duties essentially the same as the second assistant, except that his work shall be more closely identified with the out-patient department. His services shall, however, be at the disposal of his seniors on the service to which he belongs.

When the exigencies of a service require a fourth assistant visiting surgeon for a limited period, a nomination may be made to the Board of Trustees by the senior and junior

visiting surgeons on service, for the appointment of an assistant for a term of six months.

When a visiting surgeon or assistant visiting surgeon is unable to perform the duties of a service assigned to him, the service shall be offered to the other visiting surgeons and assistant visiting surgeons of the various services, in the order of seniority.

Each assistant visiting surgeon may have a vacation of two months in the year, and shall have a vacation of at least one month in the summer, in addition, if he wishes it.

Visiting surgeons shall be retired from active service upon reaching the age of sixty-five years.

While, in the opinion of the writer, the plan as detailed in the foregoing rules is not ideal, as the individuals who occupied the various positions had to be considered, yet it is believed that it is a step in the right direction. The writer believes that the following are some of the advantages of the new system:

First, it establishes a retiring age and avoids an invidious distinction being made between individuals as they reach an age where their capacity for work may be diminishing.

Second, it practically abolishes the surgeon to out-patients, and enables the youngest man connected with the staff of the hospital to have a minimum amount of surgical responsibility, under the advice and counsel of his seniors.

Third, it enables a senior to detail work to the younger men, and places the older men in a position of responsibility and of counsel.

Fourth, it gives the younger surgeons an opportunity to have a vast amount of experience by devoting a large part of their time to the hospital in their early professional life.

Fifth, it gives the older men who have gained a large experience time to devote to an individual, or an obscure, or an extraordinary case.

As a whole, it may be said that the system was constructed with the intention of placing upon the youngest member of the surgical staff the greatest quantity of work, and upon the oldest member of the surgical staff a minimum amount of labor, in order that the services of the younger men might be improved by experience and the experience of the older men be retained for the interests of the hospital.

XXI.

THE PATHOLOGICAL LABORATORY OF THE BOSTON CITY HOSPITAL.

By F. B. Mallory, M.D.

Previous to 1895 the facilities for pathological work at the Boston City Hospital had been very limited. The post-mortem examinations had been made for many years in the upper story of a small building, which was often cold in winter and always uncomfortably hot in summer. All microscopical investigations of post-mortem material and surgical specimens had been carried on for a number of years in the pathological laboratory of the Harvard Medical School. A small laboratory for bacteriological examinations of cultures from the diphtheria wards was opened at the hospital in 1893, but soon proved wholly inadequate, as the amount of work rapidly increased.

The new laboratory was opened for bacteriological and histological work in December, 1895. Post-mortem examinations, however, could not be made in the new building until September, 1896. As the laboratory has been in fairly perfect running order now for a little over a year, it is thought that a brief description of the character and aims of the work done there may prove of general interest.

Organization. The *personnel* of the pathological department has been gradually enlarged, as the amount and scope of the work to be done have increased. Since May of the present year it has consisted of seven members, as follows:

1. Visiting Pathologist.
2. Assistant Visiting Pathologist.
3. First Assistant in Pathology.
4. Second Assistant in Pathology.
5. Assistant in Clinical Pathology.
6. Senior Pathological Interne.
7. Junior Pathological Interne.

To this number should be added two voluntary assistants in surgical and nervous pathology, respectively.

The department is organized, so far as possible, on the principle of a training-school in pathology, so that each member, with the exception of the assistant in clinical pathology, is enabled, after a varying length of time, to take the place of the assistant above him. In this way only is it possible to have the work run smoothly, or to bridge over the time when one of the men, through infection or other cause, is incapacitated for work.

The men are trained in all branches of pathological work, but certain of the assistants are held responsible for certain details of the work. For instance, the general supervision of the laboratory is under the immediate direction of the assistant visiting pathologist, while the first assistant in pathology is held responsible for all bacteriological examinations. The other assistants are assigned certain branches of the work for a week at a time. By thus holding certain men responsible for certain lines of work, better results are obtained.

The different lines of work performed in the laboratory will be considered under separate headings.

POST-MORTEM EXAMINATIONS.

Much the larger proportion of pathological material is obtained from post-mortem examinations. The number of these for the last six months, from June 1 to November 30, inclusive, amounted to 165, of which 63 were made at the South Department. All of the cases naturally are not of equal interest. Those are most instructive which come to examination early, before any post-mortem changes have taken place, and in which the lesions present are due to a single ætiological factor.

Some cases demand much more thorough post-mortem examinations than others. For example, it is our routine practice to examine in all cases of diphtheria not only the organs of the abdomen, thorax, neck and head, but also the middle ears, the naso-pharynx and neighboring sinuses, and the antra

of Highmore, on account of the frequency of the acute lesions found in them. Harke's operation of dividing the base of the skull has proved of the greatest service in making these investigations, because it affords an excellent view of the naso-pharynx, and readily permits the antra of Highmore to be inspected.

In the cases of epidemic cerebro-spinal meningitis, we found it necessary to remove all of the cranial nerves, including, with the optics, the posterior halves of the eyeballs, the Gasserian ganglia, the pituitary body, the posterior root ganglia of the cord, and many of the peripheral nerves, in order to be able to study the full extent of the local and general lesions produced.

The post-mortem examinations are dictated immediately after their performance to a stenographer, and the following day the typewritten reports are read over and corrected. Later, to each report are added the results of the bacteriological examination, and a complete histological description, often with illustrative drawings, of the lesions found in the various organs.

Every hundred post-mortem examinations are bound together as a volume, and kept for future reference. The following list of the post-mortem examinations, made during the last six months, will give some idea of the character and variety of the diseases which it is possible for us to investigate. Only the more prominent lesion or lesions in each case are mentioned:

Infectious Processes.

Abscess of brain and chronic nephritis	1
Amœbic dysentery and abscess of liver	1
Anthrax	1
Appendicitis and peritonitis, acute	1
Appendicitis, pylephlebitis and abscess of liver	1
Arthritis, acute suppurative	1
Cystitis and pyelonephritis	1
Diphtheria	42
Diphtheria and measles	2
Diphtheria and scarlet fever	1
Diphtheria, scarlet fever, and measles	2
Diphtheria and tuberculosis	1
Diphtheria, scarlet fever and tuberculosis	1

Diphtheria and acute colitis	1
Diphtheria and acute enteritis	1
Empyema	1
Endocarditis, acute ulcerative	1
Endocarditis, acute vegetative	3
Endocarditis, acute and chronic	1
Endocarditis and myositis, acute	1
Erysipelas	1
Measles and tuberculosis	1
Meningitis, epidemic cerebro-spinal	5
Meningitis, epidemic cerebro-spinal and diphtheria	1
Meningitis, epidemic cerebro-spinal and pneumonia	1
Osteomyelitis and abscesses of lungs	1
Pericarditis, acute	2
Peritonitis, acute	4
Pneumonia, lobar	8
Pneumonia, lobular	3
Pneumonia, lobar and cirrhosis of liver	1
Pyonephrosis	1
Salpingitis and peritonitis	1
Scarlet fever	7
Scarlet fever, measles and tuberculosis	1
Syphilis	1
Syphilis and cirrhosis of liver	1
Tetanus	1
Tuberculosis of lungs	6
Tuberculosis of lungs and chronic nephritis	1
Typhoid fever	10
Typhoid fever and cirrhosis of liver	1
Whooping cough	2

Non-Infectious Processes and Tumors.

Alcoholism, chronic	1
Anæmia, pernicious	2
Arterio-sclerosis, general	4
Arterio-sclerosis, general, with gall stones and acute peritonitis	1
Arterio-sclerosis, general, with cerebral hemorrhage	1
Arterio-sclerosis, general, with chronic endocarditis	1
Arterio-sclerosis, general, with chronic nephritis	1
Arterio-sclerosis, general, with obliterating endarteritis and acute softening of brain	1
Cancer of gall bladder	1
Cancer of liver	1
Cancer of stomach	1
Cirrhosis of liver	2
Endocarditis, chronic	4
Ependymitis, chronic granular	1
Gangrene of foot	1
Glioma of brain	1
Leukæmia	1
Nephritis, chronic diffuse	4

Nephritis, chronic diffuse, acute	1
Nephritis, chronic, with organizing pericarditis	1
Pachymeningitis, chronic internal hemorrhagic	2
Skull, fracture of, with cerebral hemorrhage	1
Skull, fracture of, with meningeal hemorrhage	1
Skull, fracture of, with subdural hemorrhage	1
Thrombosis of femoral artery	1
Thrombosis of left sylvian artery, with cerebral softening	1
Vertebræ, fracture of cervical, with softening of cord	1

HISTOLOGICAL EXAMINATIONS.

Sections from the liver, spleen and kidneys are preserved for histological study from every post-mortem, no matter how uninteresting. From important and very fresh cases, portions of nearly every organ and tissue in the body, always including bone marrow, are saved. In other words our purpose is to make, in every desirable case, as careful and systematic studies histologically as in the past have been made macroscopically.

All pathological processes can be best studied and understood in their inception before they have progressed too far. Systematic, microscopic study of all the organs in every case which comes to post-mortem examination enables us often to get at the very beginning of lesions which do not show at all macroscopically, and which in their later stages are difficult to interpret. The most interesting line of work in pathology at present is the cell changes produced by the toxines eliminated by such bacteria as the typhoid and diphtheria bacilli. To study these cell changes perfectly, fresh, uncomplicated cases, covering various stages of the disease, must be obtained. Unfortunately, but few of the cases which come to post-mortem examination fulfil these conditions.

For fixation of the tissues, Zenker's fluid and alcohol are the common re-agents; corrosive sublimate solution, Flemming's solution and formaldehyde are used for special purposes only. All tissues are imbedded in paraffin, and, after cutting, are stained in eosin, followed by Unna's alkaline methylene blue solution, a staining combination which yields a marked differentiation of many of the tissue elements. As may be readily imagined from the above, histological work occupies a large part of the time of nearly all the members of the pathological department.

NEUROLOGICAL MATERIAL.

Aside from the cases which show acute or chronic focal lesions of the nervous system general post-mortems afford a large amount of material from the central and peripheral nervous systems which deserve investigation. This is particularly true of the acute lesions found in the ganglion cells and nerve fibres as a result of the toxines present in the general circulation in such diseases as diphtheria. Without a study of the acute degenerations thus produced in the nervous system, no adequate conception can be formed of the full extent of the lesions present in many of the acute infectious diseases. The staining methods of Nissl and Marchi are the most useful for such investigations which require a great amount of skill, time and patience.

SURGICAL SPECIMENS.

The number of specimens received from the surgical wards and Out-Patient Department during the last six months was 180, a part only of the number removed at operations. A description is written of the gross appearances of all the important specimens. The descriptions, with the bacteriological and histological reports of the same cases, are later bound into volumes.

Small pieces of tissue, sent for diagnosis only, are examined, either in frozen sections, or after hardening in alcohol. Other specimens are generally hardened in Zenker's fluid. For routine work, imbedding in celloidin and staining in hæmatoxylin and eosin are preferred, but interesting cases are imbedded in paraffin and stained in eosin and methylene blue.

BACTERIOLOGICAL EXAMINATIONS.

Cultures are made as a matter of routine at every post-mortem from the heart's blood, spleen, liver and kidneys. They are also made from any organ, tissue or cavity that shows evidence of an acute infectious process. Coverslip preparations and cultures from a given case are of the greatest importance, because, later, in the histological investigation of that case, it is indispensable to know whether the lesions

found are due to one definite organism or to an infection with several organisms.

The larger part of the bacteriological work consists of examinations for diphtheria bacilli in cultures made from the throats of the patients in the South Department. This "K L" work, as it is familiarly called, occupies a good share of the mornings of four of the assistants every day in the week. The number of cultures varies considerably from eighteen to one hundred and forty-two in a day. It averages, at present, fifty a day; but at times has averaged as high as eighty a day.

Many coverslip preparations and cultures must also be made and examined from surgical specimens, spinal punctures, pleurisies and other fluids. Fresh cultures of the typhoid bacillus have to be kept on hand all the time to use in the Widal test for typhoid fever.

There is a large and interesting field in the bacteriological investigation of certain surgical problems, such as the sterilization of sutures, gauze, operation rooms, etc. To some extent these problems have been studied by the pathological assistants, but unquestionably they would appeal more strongly to a man of pathological training who was also interested in surgery.

URINARY EXAMINATIONS.

The assistant in clinical pathology has charge of the examinations of the urine, blood and sputum, oversees the clinical clerks and house-officers engaged in such examinations, gives instruction to them when it is needed, and directs or personally carries out the finer chemical analyses required.